STATE OF MINNESOTA DISTRICT COURT
COUNTY OF RAMSEY SECOND JUDICIAL DISTRICT

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The State of Minnesota,
by Hubert H. Humphrey, III,
its attorney general,
and
Blue Cross and Blue Shield
of Minnesota,

Plaintiffs,

vs. File No. C1-94-8565

Philip Morris Incorporated, R.J. Reynolds Tobacco Company, Brown & Williamson Tobacco Corporation, B.A.T. Industries P.L.C., Lorillard Tobacco Company, The American Tobacco Company, Liggett Group, Inc., The Council for Tobacco Research-U.S.A., Inc., and The Tobacco Institute, Inc.,

Defendants.

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TRANSCRIPT OF PROCEEDINGS
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P R O C E E D I N G S.

THE CLERK: All rise. Ramsey County District Court is again in session, the Honorable Kenneth J. Fitzpatrick now presiding.

(Jury enters the courtroom.)

THE CLERK: Please be seated.

THE COURT: Good morning.

(Collective "Good morning.")

THE COURT: Counsel.

MR. CIRESI: Thank you, Your Honor. We would call Dr. Channing Robertson to the stand, please.

(Witness sworn.)

THE CLERK: Please state your name for the record.

THE WITNESS: Channing Robertson.

THE CLERK: Thank you. Please have a seat.

DR. CHANNING R. ROBERTSON

called as a witness, being first duly sworn, was examined and testified as follows:

DIRECT EXAMINATION

BY MR. CIRESI:

Q. Good morning, doctor.

A. Good morning.

Q. Doctor, you've come prepared to state your expert opinions regarding the design of the cigarette as a drug-delivery device for the controlled delivery

of nicotine for pharmacological effects?
A. Yes, I have.
Q. Okay. Before we get into your testimony itself regarding the review that you've made for the purposes of expressing your opinions, I'd like to review your education, your academic pursuits and your consulting work and background.
You're presently a professor at the Stanford University in Palo Alto, California?
A. Yes, that's correct.
Q. Are you married, sir?
A. Yes, I think so. I mean I am married.
(Laughter.)
THE COURT: We won't tell your wife.
(Laughter.)
Q. Do you have children?
A. Yes, I have a daughter who's in medical school and a son who's in college.
Q. You've been a professor at Stanford since 1970?
A. Yes, I have.
Q. Okay. Your educational background is you obtained your B.S. degree from the University of

California at Berkeley in chemical engineering with honors?
A. That's correct.
Q. You then attained an M.S. degree at Stanford University in chemical engineering in January of 1968?
A. Yes.
Q. And you then obtained your Ph.D. degree at Stanford University in chemical engineering in 1970; is that correct?
A. That's right.
Q. I'd like to just briefly review your academic experience then. You've been in the Department of Chemical Engineering at Stanford since 1970?
A. Yes, I have.
Q. You were an acting professor from June of 1970 to August of 1970?
A. Yes.
Q. You then became an assistant professor and served in that role from September of 1970 until August of 1974?
A. Yes.
Q. You then became an associate professor and were an associate professor for four years until 1978?
A. That's correct.

Q. You did a six-month stay at the Federal University of Switzerland; is that correct? In 1977, I believe it was, from January to June of that year?
A. Yes. That was a sabbatical year that I spent at the -- the ETH, the Swiss Federal Technology University in Zurich.
Q. What was the nature of your academic pursuit while you were in Switzerland, sir?

A. We had established in our laboratory at Stanford a means whereby we could measure the velocity of blood coursing through very, very tiny blood vessels and capillaries in the kidney of the rat. We were -- we were studying the means whereby the kidney is able to rid the body of waste products, and we were one of the first groups that had developed this technology. And some research folks at the Swiss Federal Institute had heard about our work and asked me to come over for six months and help them set up a laboratory to be able to do the same thing. So my wife and our daughter at the time went over there, and we -- we lived for six months and I established a laboratory for them, and then returned.
Q. And after your return you became a full professor at Stanford in September of 1978?
A. That's -- that's correct.

Q. And you've continued in that position as a full professor at Stanford in the chemical engineering department since that time; is that correct?
A. That's right.
Q. And on various occasions you've served as the chairman of the engineering department, the chemical -- the department of -- chemical engineering department.
A. Right. I've served two, a five-year term and then most recently a three-year term as chairman of the department.
Q. Now during the course of your career at Stanford, have you focused on any subspecialty of chemical engineering, doctor?
A. My emphasis has been in bioengineering, biochemical engineering.
Q. What is biochemical engineering?
A. Most succinctly it's taking the principles of chemical engineering, the tools that chemical engineers use, and -- and apply them to problems in living systems. That could be the human body in particular, or it could be in animals or even in microorganisms, any system that's alive and -- and taking in nutrients and excreting waste products for the purpose of survival. We apply our tools to

various kinds of issues and problems that are pertinent to those systems.
Q. You've belonged to various organizations during the course of your career?
A. Yes, I have.
Q. You've been a member of the American Institute of Chemical Engineers?
A. Yes. That's the -- that's the professional organization for chemical -- chemical engineers.
Q. You've also been a member of the American Society for Microbiology?
A. Yes.
Q. And what is microbiology, doctor?

A. It's basically the study of microorganisms and how they take nutrients in from the environment, how they survive and compete in the environment. And in particular as an engineer I'm interested in how we can use microorganisms as vehicles to produce new kinds of chemicals, and this is particularly relevant given the advent of recombinant DNA technology which we use as a way of redirecting the evolutionary processes themselves in order to have them produce a new suite and new kinds of chemicals that we haven't had available to us in the past.
Q. And you also are a member of the Biomedical

Engineering Society, you're a senior member there?
A. Yes, I am.
Q. Can you describe that society, please.
A. It's a society whose members cross many disciplines. It involves engineers, chemists, biologists, physicians, all of whom have an interest in studying living systems and how we can either, in some cases, develop new tools for, let's say, rehabilitation, new kinds of implants, could be artificial kidneys, artificial lungs, artificial livers, artificial pancreas, prosthetics, knee joints, anything having to do with any aspect of our ability to -- to help and -- and to -- to advance knowledge in this area. So it's a group of people that come together in meetings. It's also a way of staying in contact with people who have similar interests and helping to get our students, who seek to enter that profession, contacts.
Q. And you're also a fellow of the American Institute for Medical and Biological Engineering?
A. That's correct.
Q. And is that an organization made up of Ph.D.'s and M.D.'s?
A. Ph.D.'s, M.D.'s. It could be people with bachelor's degrees and master's degrees. Again, it's

people who have this interest in bioengineering and -- and applying their tools, whatever their tool set might be, to problems of biological systems.
Q. And during the course of your career at Stanford, have you taught in the medical school at Stanford?
A. Yes, I've -- I've taught in the medical school probably the last 20 -- 20 years, 24 years.
Q. Can you describe the type of courses that you have taught in the medical school, doctor?
A. Well I've been teaching in the physiology course in the medical school, which is taught to first-year medical students, and in particular I've been teaching a section having to do with renal physiology, which is the physiology of the kidney and how the kidney works, how it processes blood, how it removes waste products from blood both in the -- the healthy state and then also in certain kinds of

disease states.
Q. Does this deal with the subject matter of transport across capillary membranes?
A. Yes. The manner in which way the -- the manner in which the kidney works is to selectively remove certain chemicals that are in the blood across membranes in the body, and these are capillary

membranes. So if you have blood flowing through a vessel, called -- we call those capillaries, and they're very small, and you have to have a means to remove certain materials, process them, and in some cases return the materials back that you want to -- that you want to keep. So it's a -- it is an organ that is able to, in a sense, clean the blood. And of course without it, you -- you can't survive. And this is why you probably heard of folks who are on renal dialysis or dialysis machines or artificial kidneys. You've also probably heard of people who receive transplanted kidneys from donors in a way to restore their -- their kidney function if they are to -- they are to lose it.

But the fundamental way that it works is at the level of capillaries, transporting materials across these capillary walls.

Q. Have you also taught microbiology and biotechnology courses at the medical school to medical students and graduate students?
A. Yes, I've lectured in courses in medical microbiology, and I teach a graduate course each spring which is actually taught over in the medical school, discussing advanced principles in biotechnology. And the students in that class

include medical students, biochemistry students, students in genetics, immunology, pharmacology, biology, chemistry, and in engineering as well, so it's a multi-disciplinary course aimed at showing the students how they can tie what may appear to them to be disparate areas of science together to give a very powerful tool to approach important problems in -- in medical physiology.
Q. And during the course of your career, doctor, have you worked on various bioengineering projects that have medical or clinical or physiologic significance?
A. Yes. At -- at Stanford in -- in my lab, certainly the work that we have done for many, many years having to do with how the kidney functions has had a direct impact on our understanding of the -- of the kidney. I also have a deep interest in the area of biomaterials. This is trying to solve the problem of finding the magic material that we can put in our bodies that won't be rejected by our bodies so that we can replace vessels or pieces or parts of tissue, and that involves understanding how the chemical components in the body interact with these

foreign materials and then essentially trying to figure out a way to fool the body so that it won't reject these materials and it will keep them for long periods of time.

In my work that I've done outside of -- of Stanford I've consulted with many companies over the years, much of it having to do with the design of biomedical diagnostic devices. These are devices that allow physicians to measure certain chemical components in your tissue or in your blood or in body fluids that are important to making either a diagnosis or to monitoring levels of a drug that you might be -- you -- that you might be taking, and it also deals with -- just to give you a couple of examples -- and of course one of the ways I get wrapped up in this is my students go out many times and start companies, and then they'll come back and ask me to help them as they get started in developing the technology. And in one case we're working on right now that I find very interesting is when people come to the emergency room complaining of chest pains, the doctor really can't tell if the person is having a heart attack or -- or perhaps just has a bad burrito, and given the costs of medical care today, they have to assume that the person might be having a heart attack and not indigestion. And so this induces a very costly regimen that has to be

maintained and -- and put into action.

Well when you're having a heart attack, some of the cells in your heart actually die and they give some of their contents out into the blood, and if you could find those few materials that are released into the blood, you could be assured that that person is having a heart attack. So we are in fact in the last stages of developing a device where the doctor can take just a finger-prick amount of blood, put it in this device, and within two minutes have an understanding of whether or not that person is having a heart attack or has had a heart attack, and in fact where they are. Heart attacks sometimes last for long periods of -- of time; you just don't necessarily have to fall over on the floor.

And we have -- I've worked on blood glucose analyzers. If any of you know folks who are diabetic, they probably use one of the analyzers that we've -- we've -- we've worked on -- there's not that many on the market -- to be able to take a finger prick of blood, again, and be able to measure the amount of glucose that is in it so that the diabetic knows if it's time to take an insulin shot. And these are all aimed at doing this very inexpensively, very cheaply. And in fact many of these are just

discardable; you use them once and you -- you throw them away.
Q. Have you worked also on transdermal patches?
A. Yes. That's a part of -- of an aspect of what we call controlled drug-delivery systems. And a transdermal patch is an example of a controlled drug-delivery system, looks very much like a Band-Aid, and you put it on and the drug is released, a certain amount of drug for a certain period of time into the body.
Q. Have you also worked on what's called a closed loop heparin delivery system?
A. Yes. That was in the last couple of years.
When people come out of surgery, particularly vascular surgery or cardiac surgery, the physicians typically have to anti-coagulate the blood; that is, reduce its tendency to clot. And this kind of therapy can be very tricky because, as you might imagine, if you -- if you reduce the tendency to clot too much, then you can begin to bleed internally, and that's of course undesirable. And in order to ascertain the degree to which you should anti-coagulate the blood, the doctor needs to have some idea of the extent to which the coagulation process has been modified. And in this device -- and

that's usually done by a -- by a physician assistant or a nurse taking a blood sample and then making a measurement and then making a determination and then telling the doctor and the doctor going back and readjusting the regimen.
In this particular device, it just sits by the bed side. It delivers the anti-coagulant to the patient. It pulls a blood sample -- the patient has no idea this is going on other than they have an IV -- it will pull a blood sample, pump a little bolus of blood out, measure the ability to coagulate or not, readjust the pump which is putting in the anti-coagulant back into the person, and monitor the person in real time for as long as one needs to. So it's much more efficacious.
Q. And doctor, have you also worked in the area of balloon catheters?
A. Yes. This has to do with balloon -- it's called balloon angiography. You may have heard of this where if you have a buildup of material on your -- and particularly in your coronary arteries, you can take a catheter, which is a long wire, and you can place it generally in the femoral artery, it -- at the -- where your leg joins your pelvis region, and thread this up into the heart, and when it gets into

the heart you blow up a little balloon that blows up and it pushes this material back against the walls of the artery and opens up the artery. And the design of these devices is -- is very tricky because, as you

can imagine, when you're blowing a balloon up, you're also stopping the flow of blood. And so I've worked with -- with a company that designs these in ways of trying to have balloons, for instance, that are fluted, so that when they blow up, blood can still pass by. It's a very tricky -- it's a very tricky design problem and of course involves biomaterials, because you -- you don't want to have the intervention therapy actually cause worse problems than the ones you're trying to solve.

Q. During the course of your career, doctor, have you published in the peer-review journals?

A. Yes, I have.

Q. And have you published in excess of some 132 articles?

A. Approximately, yes.

Q. I'd just like to deal with some of those as they bear upon the issues that you'll be testifying to here in court over the next couple days.

First of all, in 1972, did you publish in Physiology an article entitled "A Model of Glomerular

Ultrafiltration in the Rat," and were there then a series of articles published on that issue?

A. Yes. The article you referred to is the very first article in quite a long series where we had completed an analysis -- this was a theoretical analysis -- of the mechanism whereby the kidney filters blood to be processed to remove waste components. And what was unknown at the time was how this actually happened, what are the important determinants in governing this function, because if you know the determinants, then the physician in turn can control those determinants to alter the kidney function. And what we were faced with at the time was recognizing that when you take a kidney out of one human and put it into another, it -- it doesn't get plugged back into the brain, it basically gets plumbed into the -- into the blood system and into the -- into the ureter, yet it still functions. And so being an engineer, what occurred to us that -- to myself and my student -- is that maybe it's just flows of the blood and pressures in the blood, so the mechanical aspects that really are important in controlling how the kidney works. And we developed this model, we published the model, and then went on to do a large series of experiments, a lot of

experimental work in -- in animals, to show that it indeed worked. And -- and this approach in understanding how the kidney functions is -- now forms the basis for our understanding of that particular aspect of -- of kidney function and regulation.

Q. And in 1973, did you publish in the Biophysical Journal an article entitled "A Model of Peritubular Capillary Control of Isotonic Fluid Reabsorption by

the Renal Proximal Tubule?" Now that's a long mouthful, but can you describe basically what that was about and the principles as they apply to this case?

A. I better clear that one up.

After the blood is filtered in the kidney, that filtration process removes material that you want to keep and it also removes material that you want to get rid of, so you have to separate those into two piles, as it were, and the material you don't want will end up going out to the ureter, and the material you do want now has to be taken back into the body across capillaries to get back into the bloodstream. It's now outside; it has to get back in. The peritubular capillary system is a -- is a functionally distinct capillary system in the body,

distinct from glomerular capillaries, where the fluid is taken out, and that's where material is taken back in.

So once we had studied how the material is -- is removed and then separated, we began to study how it's reabsorbed. Because if you can't reabsorb back the material that your body requires, that can also be a very, very serious -- end up being a very serious medical condition.

Q. In the course of these studies, did you need to study the architecture of membranes in order to understand the transport mechanisms that were involved in your work?

A. Yes. All this work involves chemicals and materials and substances crossing these capillary membranes, either leaving the capillary and going outside the capillary, or outside the capillary coming in, and in order to interpret our results and to have a better understanding of how that process occurs, you try to learn as much as you can about the structure of the barrier that's separating these two compartments. What is its permeability? What controls, if you will, the porosity? Why is it that larger molecules have more difficulty going through than smaller molecules? Why is it that molecules

that have a positive charge behave differently than those that have a negative charge? Why is it that molecules that might be more water-soluble have a more difficult time going through these membranes than those that are more oil-soluble? And these, again, are approaching the -- the physical parameters essentially at the -- at the molecular level as to what's controlling these processes.

Our feeling is that the more we know about that and the more we learn about it, the better we -- the better position we are to be able to react to physiologic problems that arise in the human condition and -- and be able to offer solutions that would be helpful.

Q. Doctor, when you use the term "water-soluble" or "oil soluble," what are you referring to?
A. Substances, chemicals generally will have a preference for being soluble in what we call aqueous or water solutions, and others will have a tendency to be soluble in -- in oils.
I'm trying to think -- I guess a good example is if you make an oil and vinegar dressing, you know how they separate; the oil stays separate from the -- from the vinegar until you shake it up, and then after you shake it up, it separates apart again. And

this is because the -- the oil doesn't like to be in the water. It's not very soluble in the water. Although if I take two oils, chances are they will be soluble in -- in one another. And so certain chemicals will have a preference for wanting to -- to prefer to be in water, and some will prefer to be in more oily substances, and they will actually selectively go from one to the other. If they find themselves in an oily substance and don't want to be there and there's water nearby, they'll transfer out and go into the water -- water phase.
Q. Are there terms that you use in your work that are "hydrophilic" and "hydrophobic?"
A. Yes.
Q. What -- what do those mean?
A. Well "hydrophilic" means -- "hydro" is water and "philic" is -- is loving, so water-loving or water-liking. And "hydrophobic" means water-hating or disliking water. So a -- a hydrophilic substance would be one that prefers to be in -- in water, a hydrophobic substance is one that would prefer to be more in an oily phase.
Q. Another article that you published in 1974 in the Biophysical Journal is entitled "Concentration Polarization in an Ultrafiltering Capillary." Can

you briefly describe what the subject matter of that article was, doctor?
A. When a substance is attempting to cross a capillary membrane -- say my hand is the membrane -- if the substance is having a difficult time getting through, sometimes it will pile up on -- on -- on the membrane, and this can actually interfere with the transport of other molecules that are trying, because now it -- it's -- it's sort of like getting on a subway train in Tokyo, I mean there's -- there's just too much of a resistance to get in. And so when this layer builds up, it adds, in fact, an additional resistance to the transfer and the transfer rates drop. And so we studied this effect, because in -- in the body, when you are removing materials from a capillary, particularly in the kidney, many times the proteins in the blood get pushed against the membrane. So here's the blood and you're trying to get material through, but the

proteins, which can't get through the membrane in a healthy state, get piled up, and they create kind of like a gel layer. And they -- they -- they make it very difficult for materials to leave the blood and -- and to get to where they have to to be taken to be processed. And we studied the extent to which

that that was a relevant issue to be thinking about in the way the kidney works.

Q. Another article was published in the American Journal of Physiology in '75, "Hydraulic and Oncotic Pressure Measurements in the Inner Medulla of the Mammalian Kidney." Can you briefly describe the scientific principles involved in that article?

A. Well if you recall, I said that in the kidney, blood is filtered, and then you have to recover the good things that you want and you have to dispose of the bad things you don't want, and the -- the materials that you don't want are funneled into a region of the kidney where there are essentially a series of pipes called collecting tubules, and this is where -- sort of like a drain pipe, if you will -- this is where the unwanted chemicals go. And they're finally funneled down into the ureter, which goes to the bladder, and then finally can be excreted. And we were studying what the forces were, what the mechanism was for the body to be able to selectively pull out these unwanted materials and gather them together in such a way that they could then be disposed of by the -- by the kidney, and what we were studying in this paper were the -- was a mechanistic question as to how that -- how that

happened.

Q. You also published articles on hormones released by body receptors?

A. Yes. Uh-huh.

Q. One was published in the American Journal of Physiology in 1977 entitled the "Mechanisms of Angiotensin II - Induced Proteinuria in the Rat?"

A. Yes.

Q. Can you describe that.

A. Yes. Angiotensin II is a -- is a potent hormone in our body that regulates or -- or -- or is responsible for regulating some of the permeability characteristics of these tubes where materials are crossing back and forth, and we were basically studying the effect of this particular compound on the kidney's function.

Q. You've also published in the area of materials research and how proteins react with a surface?

A. Yes.

Q. And one article in that area was published in 1977, "A Total Internal Reflection Technique for Examination of Protein Adsorption?"

A. Yes.

Q. Can you describe that briefly.

A. Well this was the -- the -- the -- the beginning

of our work having to do with trying to understand how blood reacts to the presence of foreign materials. And up until that time most people thought that to develop a proper biomaterial you needed to have an understanding of how the cells in blood adhered to the material, the red cells or the platelets or the lymphocytes, the cells that float in the blood plasma. And I think the reason people thought that is because if you put a material, foreign material into -- into the bloodstream or contact it with blood and you take it away, you see cells sticking to it. Our hypothesis was that by the time the cells arrived at the surface, the show was already over, and the real key was studying much smaller -- much smaller entities; namely, molecules, protein molecules that would reach the surface much, much sooner than the cells.

And in fact it's now well understood that when you put a foreign material into blood, the very first thing that happens within seconds is it gets immediately coated with blood proteins, and that's the surface that the cells see and decide whether or not there's going to be, for instance, a clot. And so it was -- it was an interesting and a forensics story to be able to point out that when you're

designing a biomaterial, it should be designed in such a way as to create a protein-adsorption layer that is most benevolent to then subsequent events which happen at the cellular level.

Q. And you've also published, doctor, in the area of the speed of red cells in the blood?

A. Yes. That was what we were working on when I went to Switzerland. We developed a video microscopic technique to be able to open up a part of a -- the anatomy of an animal, we used -- we used rats, and to focus in with a very high-powered microscope so that you could actually see an individual capillary.

Capillaries are -- are small, they're about, say, eight or ten microns, maybe one-tenth of the diameter of a human hair. And so we would focus in on them until we could actually see the individual red blood cells coursing through these tubes, and then, using a video taping apparatus connected to a computer, we could actually measure the speed at which cells were moving through these capillaries and deduce, then, the flow rates in these capillaries. And so for the first time we had a means of macroscopically altering the animal's ability to pump blood, say, by giving the animal a vasoconstrictor or

a vasodilator or altering its blood pressure and then actually looking at the response at the capillary level. And the reason that was important was because that's where all the transfer of the material is taking place, at the capillary level.
Q. You said that the capillary is about eight to ten microns, which is a -- one-tenth of the diameter of a human hair?
A. That's a rough approximation for the -- the one-tenth of the diameter of a human hair. It depends on whose hair, I suppose, but it's close. The idea is that it's pretty tiny.
Q. For mine it would be non-existent.
A. That occurred to me.
(Laughter.)
Q. Doctor, you've also published with regard to the application of these principles to humans, and I'd like to direct your attention to an article you published in 1981, the "Dynamics of Glomerular Ultrafiltration Following Open Cardiac Surgery." Can you describe briefly what that article was about, sir?
A. Well once we thought we had a pretty good handle on how the kidney was functioning based upon our theoretical studies and the animal models, I then

began collaborating with renal -- renal physiologists and physicians at the Stanford Hospital who were actually having to deal with patients who had serious renal deficiencies, and we began to apply the concepts that we had gathered and -- and learned about in our animal and theoretical studies to the human -- the human condition to see to the extent that therapeutic intervention driven from that point of view would be advantageous.
Q. During the course of your career, doctor, you participated on various government committees and National Institute of Health committees?
A. Yes. I've served on a number of committees in the National Institutes of Health.
Q. What is the National Institutes of Health, doctor?
A. It's a federally sponsored organization that's headquarters in Bethesda, Maryland, and it consists of a number of institutes like the National Cancer Institute, National Institute for Heart and Lung, Blood Disease, there's the Eye Institute. It's divided up -- there's an institute, I believe, now related to AIDS research and so forth. And the various institutes sponsor both intramural; that is, research that they do themselves, and then they

sponsor extramural research, which is the allocation of federal funds to universities and research laboratories to conduct research in the field of physiology and medicine.
Q. And have you received NIH funds for work that

you've conducted at Stanford?
A. Yes, I have pretty much continuously over the past, and I actually have quite a large NIH-sponsored program at the present time.
Q. Was that to establish a graduate biotechnology training program at Stanford?
A. Yes. It's used to fund graduate students who are working for their Ph.D. in a variety of fields. The money that I allocate from this program is spread out across not only the engineering, but across the fields of biology and chemistry and genetics and pharmacology, immunology and physiology and so forth.
Q. Doctor, do you hold a number of patents?
A. Well four. Not too many.
Q. Those have been issued by the United States Patent and Trademark Office?
A. Yes.
Q. You've testified in court over 27 years on three different matters; is that correct?
A. Yes.

Q. One was a toxic-waste case?
A. Yes.
Q. One involved an IUD, and you testified a couple of times on that?
A. That is correct.
Q. Were you a consultant to our law firm on that case?
A. Yes, I was.
Q. And in December of 1996, did we contact you for the purpose of consulting with regard to this case?
A. Yes, you did.
Q. Okay. And what was the scientific question that you were asked to investigate?
A. I was asked to investigate the chemical and physical aspects of cigarette design as -- as they relate to the delivery of nicotine to the human body based on the defendants' research, investigations, and specifications, and based upon my own background and training in the field of bioengineering and capability of being able to do that.
Q. And with regard to the information from the defendant, where was that information contained or set forth?
A. That was set forth in -- in their documents and in their specifications.

Q. And were there different categories of documents of the defendants that you reviewed for the purposes of conducting your investigation to render your opinions?
A. Yes, there were -- there were two -- two categories of documents. The first category was -- for which I -- I had to sign a protective order, which meant that these -- I couldn't show these documents to anyone and I couldn't discuss them with anyone, my colleagues or -- and I had to keep -- keep

them under my control at all times, and then there was yet another category of documents which the defendants considered to be so secret and so confidential that they were main -- they were and are maintained in two rooms at Mr. Ciresi's law firm, and these rooms are electronically armed and they're kept locked, and the only way I could review those documents was to come to Minneapolis and sit in one of the two rooms and review them there. I wasn't allowed to take anything out of the room, none of those documents could be copied, and any notes that I took had to remain in the room. Those were the two categories.

Q. Doctor, I'd like to direct your attention to drug-delivery device designs, and I'd like you to

relate to the jury and to the court your experience in designing drug-delivery devices by way of examples that you have been involved in during the course of your career.

A. Well my involvement in -- in controlled drug-delivery systems goes back to my very early days at Stanford when I engaged in a consulting relationship with a company that had just been formed in the Stanford Industrial Park. It was called Pharmetrics at that time; it was then subsumed into another company known as Alza Corporation. And I in fact spent my first -- my first summer after the academic year at Stanford working on a drug-delivery system which had involved, for instance, the use of --

Maybe I should just point out what a drug-delivery system is just briefly. It is a system that releases a drug for -- for therapeutic purposes, generally at a controlled rate and in a controlled amount for a known period of time. And I worked on one having to do with the release of progesterone into the female uterine cavity as a means of an alternative to oral birth control, as a means of contraception.

I worked on another having to do with the

release of a drug, pilocarpine, into the eye for people who have glaucoma.

Worked on the first transdermal system -- that's one of these little patches -- for the release of a drug known as scopolamine, which is used to combat motion sickness. And later that technology has been used to -- in other kinds of patches, such as nitro-glycerin patch to reduce the pain of angina, heart pain, another one to release clonidine, a hypertensive -- anti-hypertensive agent for people with high blood pressure. I worked on a little pump that you would strap to your arm and there would be an IV tube into a vein, and the material in this little pump would be passed through the tube into your vein. You could wear this for a period of about

a week. This was used primarily for folks -- for folks who are on cancer chemotherapy where they could be receiving a very small dose of material constantly over a long -- a long period of time. And I worked on another system known as Oros, which is the oral osmotic delivery system. There is a product on the market called Accutrim, which is an appetite suppressant, and you might see on the packages it will say "timed release," something of that nature, and it's based on that technology, which is also used

now in the veterinary business as well as a means of releasing drugs an over long periods of -- well reasonable periods of time at known dose rates.

Q. Do designers of drug-delivery systems utilize certain elements in designing the drug-delivery device or system?

A. You know, all these systems have what I call design paradigm; that is, if you're going to make a car, you're going to have wheels, going to have an engine, going to have seats, going to have a steering wheel. And a controlled delivery system has similar kinds of elements. The basic element is what we call the platform, and that is the -- the -- the -- the -- the thing, if you will, or the material or the -- or what contains the device. We call it the platform. And then on this platform you mount the various elements of the device, and the first thing you need is a reservoir, you need a container to hold the drug. There's many ways you can do that, but just in an abstract sense, you need this container to hold the drug.

Then you need a -- a means to permit the drug to leave the reservoir and reach the outside world, if you will, so that it can leave the platform and be delivered to the -- to the recipient, to the patient.

Then you need a rate controller. You need something that sets the rate at which the drug can leave the reservoir, go through the portal and -- and leave. So that sort of sets, if you will, the dose rate.

Then you need an energy source. You need something that is going to cause the drug to want to leave the reservoir, pass through the portal and through the rate controller to reach the outside world.

There's one other element, but it's -- that we would like to have on these devices, but really to date we haven't been very successful, and that is a feedback control mechanism where the device itself can monitor the level of the drug and react to the level and reset the rate controller if the drug gets too high or gets too low.

And an example that many people have been working on is that of the delivery of insulin. We can make a device that delivers insulin at a fixed

rate, but your body doesn't need insulin at a fixed rate, it needs it in relationship to the blood glucose levels. So if your device could sense blood glucose levels and then release the appropriate amount of insulin, you'd have what we call a closed

feedback loop system. And really to date that's -- that's the fight, it's almost, you know, the Holy Grail of controlled drug delivery design.

And that's not to say that there aren't a number of drugs that you can just simply deliver at a constant rate or at some rate for a fixed period of time and you'll do just fine, and there are many such of those devices out on the marketplace today.

Q. Doctor, could you step down for a minute and use the ocular device that you worked on to depict the various elements of a drug-delivery system? And we'll give you the write board down here.

A. Okay.

Q. Before you -- I'll move over here, doctor, so I don't block you.

Before you draw the elements, is there a concept known as a therapeutic window in a drug-delivery device?

A. Yes. It's a therapeutic window or -- or dose window or dose range that's critical to the design of these devices.

Q. Can you describe what that is, maybe through the use of the write board.

THE WITNESS: Can you see it from that angle?

(Affirmative response from the jury.)

A. I'm going to make a -- start out by making a plot of -- let's call it drug concentration on this axis.

Q. You're now writing on the vertical axis?

A. Right. The word "drug concentration," this -- this is its -- when you deliver a drug, what you want to do is achieve a certain concentration of that drug at its site of action; that's really where you're interested in it, where that drug is having its effect. And --

MR. CIRESI: Doctor, if I might interrupt you just a minute. I'm going to put an exhibit sticker on here for illustrative purposes, Your Honor, Exhibit 25009, so the record will reflect what exhibit is being referred to in the testimony.

I'm sorry, doctor, please continue.

A. Now drugs are -- are characterized as having -- generally, with most drugs, reach a level that's too high of a concentration, and the drug can start exerting undesirable side effects or become toxic, and so in designing one of these devices, generally you're -- you're cognizant of the existence of some maximum that you don't want to exceed because there's going to be undesirable side effects or toxic

effects. There's also a minimum. Clearly zero is a minimum; there's no drug and there's no effect at all. But typically with drugs there is some threshold level that has to be met before the drug begins to elicit the -- the response that you're interested in. So there's a -- there's a lower limit or what we call a threshold. And so what you want to do is you want to operate your system such that the drug is delivered in between these two green lines. You would like it above the minimum and below the maximum.

Now if we plot time on this other axis, the horizontal axis, now we can begin talking about achieving certain concentration for certain period of time. And the reason that we began researching and developing devices back in the 1970s that could do this is because one of the problems physicians have with patients is called lack of patient compliance. I mean I wouldn't want to say any of you have done this, but how many have popped three aspirin instead of two even though the bottle says two, but maybe three will make you feel better soon, that sort of thing. So you see in that kind of approach you have to be careful in how you dose out medicines, because if you dose out medicines that truly have a lethal

maximum, you have to be careful that patients can't self-administer and get themselves into trouble.

And typically, you know, the way we take drugs is either by injection or by pills, and we tend to be taking them periodically, every four hours, every six hours and so forth, and so the drug concentrations that we have typically in our bodies with this kind of a therapy is at time zero there is no drug, and then let's say you take your first pill, and your -- let's say your blood concentration rises, and then it begins to fall. Then you take your next pill, it rises again, falls. Or your next injection. So this can apply to any kind of a -- of a drug.

But you see there are regions here where the concentration has fallen below the threshold and you're not receiving the benefit of the drug at that -- under -- under those circumstances. Likewise, what is even a more disturbing possibility is if you rise above the maximum, and potentially you could actually rise below the -- go below the minimum and have this kind of a possibility happening, and now you are going above the maximum and falling below the minimum, and so you have regions of ineffectiveness and you have regions where there's a potential for toxicity or adverse effects.

Now because of this, many of the drugs that are

on the market, if not most of them, have a very wide window so that the possibility of exiting this window is minimized. So the notion with a drug-delivery system -- I might run out of colors, so I'll go with black -- is what if we could have an engineered device which allowed us to rise up somewhere in this window and ensure that we stay in that window for a given period of time? And this is what gave rise to this notion that if you could somehow have the device that releases the drug at a prescribed rate for a prescribed time located somewhere in or on the body, then we could end up with a -- a therapy which would allow us to ensure the maximum wouldn't be exceeded and the minimum wouldn't be reached until the therapy was ended or over.

Q. Now can you describe in the context of either the transdermal patch that you worked on or the ocular device how the elements of the drug-delivery design are incorporated into a specific drug-delvery device?

A. Would you like me to do both or just one or the other?

Q. Either one. Whichever one you want.

A. Well I'd like to do both, but I don't know if

the people have the patience for --

Q. Why don't you start with the one that's most informative.

A. Okay. Let me do the patch, because it's probably the one you're most -- if you've seen one of these you'd probably -- you might have seen one of these patches. The first one was the scopolamine patch, and it was worn behind the ear. There was a little -- looked like a little Band-Aid. The reason it was here is because your skin on your body is about as thin here as it is anywhere else, and so since the drug has to go through the skin, you want to minimize the -- the barrier that it has to go through.

So the way this was manufactured was, first, to take a material -- I won't get into the details of the material, but take -- take a material that would act like a little molecular sponge, if you will, in which the drug, in this case some scopolamine, was incorporated. So that the image that you should have in your minds is that essentially the drug is sopped up into this -- into this material. Then a back -- a backing is put on this, or an overwrap if you will, to contain this element. And this little element that holds the drug, if you were to see it, it would

look like a -- much like a piece of Saran Wrap or wax paper. It's just like a -- would look like a film. And then you could just coat a backing onto it, usually like a foil coating.

Have you seen potato chip bags? They actually have an aluminized coating to -- so that air won't

come in and foul the potato chips, and then there's another plastic coating. So we have a technology to lay these films down one on the other. So we put a backing on this. Now --

So we have a reservoir. Now we need something to allow the drug to escape, a portal, and we need a rate controller. And that's done in this device in one step, by putting a -- what we call a rate-controlling membrane, which I show here in green. So we have the reservoir and we have the rate controller, and this green piece of film also serves as the portal.

And the way you should think of this film is that by controlling -- I'll just say it sort of by description. If you can control, let's say, the sizes of the holes, if you will, in this membrane, and the number of holes in this membrane, then that will control how fast the red drug can move through it. So if this was totally impermeable, no drug

would leave; and if I make it more and more permeable, then more and more drug can leave. And the rate at which it leaves will be set by just how permeable this green sheet is. So by adjusting the permeability of the green sheet, I cannot only provide a portal, a route for the drug to leave -- it can't leave out here because this is covered with a backing, it's impermeable, can only leave out through the bottom.

Now if this was going to be a transdermal system, then I need to attach it to the body, and so we attach it to the body like a Band-Aid, but that requires an adhesive, so we have to then coat an adhesive. Now the adhesive is -- is not part of our elements, but it becomes part of this device because of the manner in which it's used. And in this particular case we took advantage of this adhesive, because if you put one of these devices on -- it looks just like a Band-Aid, you peel the backing off just like you do on a Band-Aid to stick it on your skin. You have to wait a while before the drug begins to permeate through the rate controller and through the -- whatever adhesive there is there and then through your skin and finally get into the blood, so there is a -- a time delay, if you will,

after application, and then you have to wait until the blood level rises sufficiently to get above the minimum threshold before you start receiving a physiologic effect.

I can remember the discussions we had about people climbing on a boat and saying, "Oh, put it on," and expecting that, you know, they won't be sick. But it takes a while for these to begin to work. So we actually incorporated some drug in the adhesive material so that it would prime the system so that when you put it on, you immediately were

starting to get some -- some of the drug, and then it would be followed by the drug that comes out of the reservoir.

The energy source here, which is the only element that we haven't discussed, might be a little obscure, and that is: What is driving the drug out of the reservoir? And the process that does that is called diffusion. And I think the best way to describe diffusion would be if we were to take a mothball and put it back in this corner and I had everybody in the courtroom raise their hand when they smelled the mothball, I think you'd all probably guess that the folks closest to the mothball would raise their hands first, and then you'd see hands go

up, and I guess you're maybe one of the furthest ones away, and then his hand would go up last. And what you're perceiving is the process of diffusion. What is it that's causing the -- why do the vapors from the mothballs do what they do?

Well they're concentrated over in the corner, so you have a high concentration of the vapors from the mothball and they're dispersing by diffusion throughout the room, and the end point of that would be the entire room filled rather uniformly with the vapors from the -- from the mothball.

If I were to put a drop of brilliant red dye into a pan of water, we all know that it just doesn't sit there -- when you make Easter eggs, for instance -- it spreads out, it diffuses out until it's uniformly distributed throughout the entire body of water. And this process of diffusion is a -- is a process that occurs in our everyday life all the time. It's this tendency of substances that are in regions of high concentration to disperse themselves out and so they're evenly distributed throughout whatever space they can find themselves in.

So here we have the drug concentrated in this reservoir, and once we open it up to the outside world, since it's in high concentration here and it's

in low concentration in the body, it will begin to move from the reservoir into the body until the concentrations are essentially equalized, and then the -- it will come to a halt.

This in fact is the process that drives oxygen in our lungs into our blood. If you've ever thought about it, we breathe in. How is it that the oxygen has this tendency to go into the blood and there's a reverse tendency of the carbon dioxide that's being brought to the lungs, the waste product of metabolic processes, that has to be excreted? It's the same process. In the lung, in the air spaces, you breathe in, the oxygen concentration is high; the blood on the other side of the lung capillaries, the oxygen concentration is low because it's been depleted. It's been through your body, it's now come back to be

rejuvenated. So the oxygen flows downhill from a high concentration to the low concentration in the blood and it's taken up. Likewise, the carbon dioxide, which has a high concentration in the blood and relatively low concentration in the lungs, flows out of the blood into the lungs and it's exhaled.

So the very same process, from mothballs, this device, and the lung, are operative. It's called diffusion.

Q. Thank you, doctor.

THE COURT: Let's take a short recess at this time.

(Recess taken.)

THE CLERK: All rise. Court is again in session.

(Jury enters the courtroom.)

THE CLERK: Please be seated.

BY MR. CIRESI:

Q. Do you have your microphone on, doctor?

A. Yes, I do.

Q. Okay.

MR. CIRESI: Your Honor, we'd offer for illustrative purposes Exhibit 25009, which was the sketch that the doctor drew.

MR. BERNICK: No objection, Your Honor.

THE COURT: Court will receive 25009.

BY MR. CIRESI:

Q. Now doctor, we've been talking about a drug-delvery device. What is a drug?

A. It's a substance that elicits a pharmacological response.

Q. And what is a pharmacological response?

A. It's the interaction between the -- the drug and its receptor site in the human body and the

alteration in the function of the human body that ensues.

Q. I'd like to direct your attention now to nicotine. What is nicotine?

A. Nicotine is an organic molecule that is synthesized in -- for instance, in plants, various kinds of species of plants.

Q. Is it pharmacologically active?

A. Yes, it is.

Q. Is it toxic?

A. Yes, it is toxic.

Q. Can you draw for us the chemical compound of nicotine?

A. Yes.

Q. For purposes of identification, I'll put an exhibit tab on, which is 25010.

A. A large part of our world is made up of organic molecules: wood, gasoline, fuels are organic molecules, and nicotine is in the world of organic molecules. And it's synthesized as part of a metabolic factory or engine of a -- of a plant

material like the tobacco plant, and it's composed of carbon atoms. This is the beginning of the molecule, and it has -- so the C stands for carbon, the same kind of material that's used to make tires black and

that you find in pencil lead.

Q. What are those double lines?

A. You can think of a --

All molecules are atoms connected together much like a Tinker Toy set, and the lines I've drawn connecting the atoms of carbon, in this case, to the atom nitrogen, nitrogen is found as one of the primary components in air, it's called a chemical bond, so this is like the stick in a Tinker Toy set that holds two little pieces together. And to take a molecule apart, you have to disconnect that bond and to form a molecule you have to connect it, and part of what living systems do is to take in carbon, normally that we eat, and other atoms into our body and reassemble them into things like tissue and blood and cells and hair, all the things we need to survive. It's a part of what life is all about, is the disassembly and the reassembly of -- of molecules.

So carbon is an element that always would like to be hanging on to four other things, and that's why, if I get this right, you'll find that there's always going to be four little sticks or bonds coming out of carbon.

Hydrogen, on the other hand, only has one, so it

will make one bond to something and that's all.

Nitrogen likes to attach to three other atoms or have three bonds, so it uses two of them to attach to this carbon.

And as we move through the molecule, this is called a pyridine ring, this is a pyrrolidine ring -- those are terms we use in chemistry. It's attached to this other structure which has four carbons and another nitrogen. I need to add some hydrogens over here to -- to these. And you'll see in this case the nitrogen has its arms, if you will, attached to these two carbons and then to another carbon. But remember, the carbon's going to have four, and in this case one's to the nitrogen and three are to -- three hydrogens attached to this carbon.

Now I just want to be sure I've done this right, so I want to check by checking the molecular weight which I know the answer to, just to make sure I don't leave anything out. So I have one, two, three, four, five, six, seven, eight, nine -- we have ten carbons, we have two nitrogens, one, two, three, four -- 14 hydrogens, and the molecular -- the atomic weight of carbon is 12, so this ten times 12 is equal to 120, and we have two nitrogens that have an atomic weight

of 14, so that gives me 28, and we have 14 hydrogens that have an atomic weight of one, that will give me 14, and that adds up to 162. And this is called the molecular weight of this molecule.

Nicotine -- which obtained its name, by the way, by a Frenchman, Nicot, N-i-c-o-t, who was the French Ambassador to Portugal that came upon some seeds, as I understand it, of the tobacco plant and grew them and was one of the people that was in the history of tobacco and its emergence in society, and so they named the molecule nicotine after him. So this is an organic compound, and in this particular case, as we -- as we will learn, it has certain physiologic effects when taken into the body.

Q. You said it can be toxic. Can it be lethal or poisonous?

A. Yes, it can be. It's thought --

Evolutionarily you have to ask the question: Why would a plant make this? Typically biology is -- has had billions of years to hone and perfect the suite of molecules that it needs; that is, a biological system needs in order to survive or compete in a hostile environment, which we all basically live in. In this case for the tobacco plant or species of plants that produce this

material, it's synthesized in the root structure, and then it migrates through the plant up into the leaves. And it's thought -- at least one of its properties is to provide sort of a natural insecticide resistance to the plant against predators that may come and try to attack the plant or eat it.

If nicotine is purified from the plant -- and it can be, and in fact there is a -- or at least there has been a market for nicotine commerce, it's used as an insecticide and as an fumigant -- it has a -- a lethal dosing in man of roughly about 40 milligrams. Now of course this would differ from person to person depending on your body weight, your size, and sort of the level at which this becomes toxic to you, so this is just a -- a round figure.

And 40 milligrams isn't very much. To give you an idea, one pound of -- if you're thinking of a pound of something -- has 454,000 milligrams in it. So this is but a very small fraction of one pound. There's approximately eleven thousand equivalent lethal doses in a pound of pure nicotine.

Q. How many milligrams of nicotine does the average cigarette -- the range of an average cigarette have?

A. It would range, as there are ranges, let's say eight to -- eight to 15 milligrams, something in that

range, in an individual cigarette.

MR. CIRESI: Your Honor, we'd offer Exhibit

25010 for illustrative purposes.
MR. BERNICK: No objection, Your Honor.
THE COURT: Court will receive 25010.
BY MR. CIRESI:
Q. Now doctor, based on your experience and training and expertise and your investigation from this case, do you have a opinion to a scientific certainty as to whether nicotine is a drug?
A. Yes, I do.
Q. And what is your opinion?
A. Nicotine is a drug.
Q. Did the defendants, based on your review of their documents, internally consider nicotine as a drug?
A. The defendants considered nicotine to be a drug.
Q. To your knowledge, at any time prior to the commencement of this lawsuit in August of 1984, did any of the defendants publicly -- publicly admit that the cigarette was a drug-delivery device?
MR. BERNICK: Objection, Your Honor, lack of foundation.
THE COURT: Sustained.
Q. You've reviewed the defendants' documents in

this case?
A. Yes, I have.
Q. You reviewed the literature?
A. Yes.
Q. And to your knowledge -- I'm just asking you based on your knowledge -- did you see any indication that the defendants publicly admitted that the cigarette was a drug-delivery device prior to August of 1994?
MR. BERNICK: Same objection, Your Honor.
THE COURT: No, you may answer that.
MR. CIRESI: You may answer.
A. I know of no admission, public admission by the defendants that a cigarette is termed to be a drug-delivery device.
Q. Internally did the defendants acknowledge that the cigarette was a drug-delivery device?
MR. BERNICK: Same objection, Your Honor.
THE COURT: You may answer that.
A. Yes. In their documents they admitted and expressed that a cigarette is a drug-delivery device.
Q. Internally, based on their documents, did they state they were in the drug-delivery business?
MR. BERNICK: Same objection, Your Honor.
THE COURT: You may answer that.

A. In their documents they expressed that they were in the drug-delivery business.
Q. Now these documents, doctor, were written by various scientists of the various defendants?
A. Yes. Various employees of the defendants, including their scientists.
Q. With regard to the opinions that you're

expressing in this case with regard to nicotine, did the defendants' scientists internally agree with those opinions?
A. Yes.
MR. BERNICK: Your Honor -- I'm sorry. Could I have just a continuing objection on lack of foundation until we know what particular documents are being placed before this witness that he has reviewed?
THE COURT: Yes, you may.
MR. BERNICK: Thank you.
BY MR. CIRESI:
Q. Did the defendants' scientists study nicotine's effect on the human body?
A. Extensively.
Q. Did the defendants' scientists state that their product was nicotine and not tobacco?
A. Yes. They stated that their product is

nicotine, not tobacco.
Q. Did any of the defendants' scientists express an opinion that without nicotine there would not be a cigarette industry?
MR. BERNICK: At this point the questions are also leading. Object to the form.
THE COURT: They are leading, counsel.
BY MR. CIRESI:
Q. What if anything did the defendants' scientists express with regard to whether or not there would be a cigarette industry without nicotine?
A. They said in their internal documents that, in the absence of nicotine, there would be no cigarette business.
Q. What if anything did the defendants' scientists express with regard to the threshold levels of nicotine in a cigarette?
A. They indicated a clear awareness that there was and there is a threshold level of nicotine below which it will not have its desired pharmacologic response.
Q. Doctor, can you direct your attention to volume one of the documents in front of you, on the side, and specifically Exhibit 12408, which is already in evidence. This is a confidential RJR document on the

subject of "RESEARCH PLANNING MEMORANDUM ON THE NATURE OF THE TOBACCO BUSINESS AND THE CRUCIAL ROLE OF NICOTINE THEREIN," authored by Claude Teague on April 14th, 1972.
Is this one of the documents that you reviewed for the purposes of preparing for your testimony?
A. Yes, it is.
Q. Can you direct your attention to the first page of that document.
A. Yes.
Q. If you can direct your attention to the first part of page one, and I want to read a couple parts

and then ask you some questions with regard to a drug-delivery device.

"In a sense, the tobacco industry may be thought of as being a specialized, highly ritualized and stylized segment of the pharmaceutical industry. Tobacco products, uniquely, contain and deliver nicotine, a potent drug with a variety of physiological effects."

And if you could direct your attention down to the same paragraph starting about seven lines from the bottom, "Thus a tobacco product is...." Quote, "Thus a tobacco product is, in essence, a vehicle for delivery of nicotine, designed to deliver the

nicotine in a generally acceptable and attractive form. Our Industry is then based upon the design, manufacture and sale of attractive dosage forms of nicotine, and our Company's position in our Industry is determined by our ability to produce dosage forms of nicotine which have more overall value, tangible or intangible, to the consumer than those of our competitors."

Now with regard to the cigarette, doctor, and these two phrases of Mr. Teague, how do those relate to the elements of the drug-delivery system that you have referenced earlier in your testimony?

A. Dr. Teague has affirmed the view of his company, R. J. Reynolds, and even that of the industry, that -- that they con -- he considers themselves to be a pharmaceutical industry, an industry that is embracing a -- a drug to be delivered to the recipients, to -- to humans, and that that drug has to be delivered in an appropriate dosage form in order to achieve the -- the effect that it's intended to have. So he's basically describing an industry that is -- that is in the business of producing a -- a -- a product, a drug-delivery device intended for that sole purpose,. The drug in this case is nicotine.

Q. And can you direct your attention just up a little bit in that same paragraph to the following words, "His choice of product...," do you see that?

A. Yes.

Q. "His choice product and pattern of usage are primarily determined by his individual nicotine dosage requirements and secondarily by a variety of other considerations," and then he lists them.

I want to direct your attention to that first part of that sentence. By "His individual nicotine dosage requirements," what if any relationship does that have to the elements of a drug-delivery device system that you were referencing earlier in your testimony?

A. The key issue here is that the user -- in this case, the consumer of a cigarette -- obtains and elicits a pattern of usage that ensures that the drug

will be taken in in such a way as to keep it in this dose range window that we were talking about. Obviously, if it went below that, there wouldn't be the biological or physiologic effect that was intended, and that that is the -- that is what primarily is involved here; that is, individual nicotine dosage. Secondary to that are things like flavor and irritancy and so forth.

So the primary issue here that he brings out is that it's the ability to take in an appropriate amount of this drug and to establish the dose range window and to maintain it.

Q. Could you direct your attention, then, doctor, to page three of this exhibit, 12408. I'd like to direct your attention to the bottom portion of that page, which carries on over to the next page, four, and I quote, "If nicotine is the sine qua non of tobacco products and tobacco products are recognized as being attractive dosage forms of nicotine, then it is logical to design our products -- and where possible, our advertising -- around nicotine delivery rather than 'tar' delivery or flavor. To do this we need to develop new data on such things as the physiological effects of nicotine, the rate of absorption and elimination of nicotine delivered at different frequencies and by different routes, and ways of enhancing or diminishing nicotine effects and 'satisfactions'."

During your investigation of the defendants' documents, did you ascertain whether the defendants did in fact research the rates of absorption and the physiological effects of nicotine and the ways of enhancing or diminishing nicotine effects and

satisfactions?

A. There -- there is evidence in all the defendants' documents that they were engaged in these kinds of activities for many, many, many years.

Q. I'd like to direct your attention to the word "the rate of absorption." Is that absorption in the lung?

A. That would be referring to uptake, yes, --

Q. Okay.

A. -- in the lung. Because when you inhale a cigarette, that's where the nicotine is taken up primarily.

Q. Now Dr. Hurt described sort of the gross anatomy of the lung, and I'd like you, if you could, to step down once more and to address yourself to the microanatomy of the lung where absorption takes place of the nicotine, if you would, doctor.

A. May I just show a little clip here first?

Q. Absolutely. And let me move this --

You should have control of it now.

A. I understand that this is a clip that you may have already seen, but if you don't mind, I'll just

go through this once again to get you oriented as to the -- the lungs, the trachea, which branches into the bronchi, and now out comes a section of the lung

tissue, which has a very spongy kind of consistency to it. And as we go to higher and higher magnification, we see that the small vessels, the bronchi, which have descended from the larger vessels, begin to show evidence of these little alveoli structures. These are the gas-exchange units in the lung that have evolved as a physiologic means to very efficiently transfer oxygen and carbon dioxide across the barriers.

And as we hone in on this alveolar structure, there's about three hundred million of these in the human lung, and as you can see, the outside of these structures are covered with capillaries that are carrying blood that is low in oxygen concentration, shown in -- in blue, and is being reoxygenated to be carried back to the left side of the heart to be pumped out into the systemic circulation.

Now as we break away and go inside an alveolar structure, you can see where I put the arrow that it has a very, very thin wall, that the capillaries coat it in a way, embrace the structure, and inside you have the air space which is fed through the alveolar ducts. You can see two of them in the -- in the background there. Little bit like grapes hanging on the end of a -- of a stalk. And it's -- it's in this

region that the exchange of oxygen into the blood occurs by traversing this -- this barrier, the capillary barrier, in order for the oxygen that's been brought in through a breath, to take it and put it into the blood plasma and then where it's taken up by the -- the red cells.

Now the reason it's taken up by the red cells is because the solubility of oxygen in water or in the plasma in which the red cells float is very, very slow -- low, and it doesn't have -- our blood doesn't have the capacity to absorb enough oxygen just by dissolving the oxygen in solution, and so red cells have in them a substance known as hemoglobin.

(Juror coughing, and bailiff hands him a glass of water.)

THE WITNESS: That's all right, I'll take a break while you --

A. Hemoglobin is a protein that binds oxygen, so you might think of it as an oxygen vacuum cleaner, and it can actually concentrate the oxygen to levels higher than you otherwise would have if you just dissolved it in blood. So it's a very interesting transport system. Likewise, carbon dioxide will be taken from the red cells and then moved into the alveolar space.

What I want to point out here is, as we can see, the oxygen is traveling from the alveolar gas space into the blood because it's going down its concentration gradient; its concentration is higher in the gas than it is in the blood, and so it has this tendency to move from the gas across the wall and into the blood. So having said that, I can focus more in for you on the alveolar structures.

MR. BERNICK: Your Honor, at a certain point I think we're going to object -- maybe now is the right time. This really is cumulative. All this was gone through in connection with Dr. Hurt's testimony, the same points, the same visuals, the same substantive testimony. It's cumulative.

THE COURT: Well the objection is overruled. You may continue, doctor.

MR. CIRESI: We will mark for purposes of identification Trial Exhibit 25011.

Q. And I'll give you some markers, doctor. If you could describe now the microarchitecture of the lung which will form the basis of your further testimony as we move through the defendants' documents.

A. The lung and its attendant structures is a highly evolved system to transport gases, as we've been discussing, and it -- it begins with the intake

of the gases through the mouth or through the nose, through the nasopharyngeal region it's called, through the larynx and into the trachea. The trachea is about the size of your thumb, and it divides into two, and that divides into two again, and that divides into two again, and so you have a branching network almost like an upside down tree -- and so forth. So this branching -- as this branching structure evolves, the diameters of the tubes become smaller and smaller and smaller. Starts out, as I said, about the size of your thumb, and after about -- and in fact for about the first eight to 13 generations there is cartilage material around the tubes so that they retain their shape and don't collapse. Finally, when they become small enough -- and this is called the -- the bronchi, and the bronchioles -- when you have this transition from what's called bronchi to bronchioles, the cartilage begins to disappear and you finally get to a region called the terminal bronchioles. And so you have a section of the lung which is designed to transport the air through a series of tubes called the conducting airways, and it keeps splitting two by two by two by two until you finally find yourself down in the terminal bronchioles, the respiratory

bronchioles, the alveolar ducts and the alveoli themselves. And when you're down in these lower reaches and deep reaches of the lung where now the

tubes have become on the order of about 0.05 centimeters in diameter, and that's about five hundred microns -- a micron is a millionth of a meter, and that would be, you know, roughly, again, several human hairs together in size, very, very small tubes -- this results in reaching the alveolar structures, of which, as I said, there's about three hundred million of them.

Now the reason that it's evolved this way is to be able to take this airflow and split it and split it and split it and yet reduce the diameter of these vessels in such a way as not to create a huge resistance so that it will be very difficult to breathe but at the same time to be able to spread the gas out over a very, very large surface over which the gas exchange can occur. So this is what physiologically has evolved through nature, and the lung area in our lungs is measured in the tens to around hundred square meters, which is an enormous -- maybe 30 by 30 feet or even -- or even larger in terms of the area. But this then gives the gases plenty of surface area over which to exchange,

the oxygen to go in and the carbon dioxide to -- to come out.

Now when you leave the conducting airways, after you've left sort of the nasal/throat region and conducting airways, you're now down into what's called the respiratory region, and what I'd like to do is take you into an alveoli and see what we find. And I'm going to have to use another piece of paper to do that. And I'll draw for you a section of the wall of the alveolar structure. This will be highly -- highly schematic. So this is where the -- the gas or the -- or the air is.

Q. We have designated that for illustrative purposes 25012.

A. Now these alveoli are made up cells, cells that are connected together in such a way as to give structure, to give a shape. And you can think of it as these alveoli, these little -- little grapes, if you will, as being somewhat spherical for purposes of -- of our discussion.

And I'm now showing you the gas phase and I'm showing you just a little bit of the cross-section as if we were inside it, and what I'm showing here is just a -- an individual cell called an endothelial -- epithelial cell. And this cell has a nucleus, which

has its DNA in it and its -- its -- its machinery that is the biological machinery needed in order to carry out its functions. And you can see it's shaped much like a little plate. And then there's another one here, there's another one here. So if you --

My view is if you were inside the alveoli, it would look somewhat like being in -- you know, you have those big theaters here with the round roofs,

and you can look up and you can see sort of a tiled effect? That's kind of what you might imagine. You'll see these cells that are attached together much like tiles are on a floor. This is what you would -- this is what you might see.

And then on the back side of these cells is material of generally higher molecular weight, that is large molecules that kind of form some structure on which these cells sit. This is called the basement membrane or the interstitial region. I guess you might consider it to be a little bit like the grout that the tile is set in. And then on the other side of that is another kind of cell called the endothelial cell, and then we have the blood, and the blood is contained within one of those capillaries that we saw schematically represented, and it's sweeping by over these cells.

Now to give you an idea of the scale, which as an engineer I always like to think of how -- how do you get a sense of how big or how small something is? And to tell you that this is .2 to .6 microns in wall thickness might not be as illuminating as if I tell you this: Imagine if we were in an alveoli and it's three hundred feet across, about the size of a football field. Can you picture that, where a huge, round sphere is about the size of a football field? This wall would be maybe six inches thick, on that -- on that scale; maybe a little less, maybe a little more, but on that order. So it's a very, very -- almost like a egg shell; very, very thin. And of course that makes sense because you're trying to exchange gases from this space into the blood and reverse as fast as you can. There's only so much time available as this blood comes sweeping through to pick up the oxygen that's being provided into these, get to saturation, and take it to the left side of the heart and deliver it to the body.

So in actual units, the diameter -- they vary, of course, but roughly about three hundred microns. And all I did was I took the three hundred microns and say imagine it's three hundred feet, so you can get the idea of a scale, and this distance here, the

wall thickness, is about 0.2 to 0.6 microns, or if this was three hundred feet, this would be about .2 feet, so it would be a couple of inches, and this would be .6 feet, which would be about half a foot, so -- or a little larger than that, seven or eight inches. So it gives you an idea. What I want to communicate to you is just how thin this -- this membrane is.

Now in addition --

Q. Doctor, can I interrupt you one second there?

In terms of other body membranes, how thick is this?

A. Well it's one of the thinnest, it is the

thinnest capillary membrane in -- in the body. And of course, again, it's evolved to be that way for the purposes for which it is -- for which it's intended.

Now the inside of this alveoli is -- has some fluid in it. Of course you don't want to have too much fluid because then your lungs would tend to fill with fluid, and of course that would be -- that would have negative consequences. But nonetheless, since cells live in a -- kind of a wet environment, there is a fluid film which is called the hypophase, which is very, very thin, it's about, gee, on the order of a tenth of a micron or so, and it appears to be very

viscous; that is, sort of sticky, so it's -- it doesn't flow very well. But it's contained primarily of water and other large organic molecules.

And then on this film there are another set of molecules that -- that occur on the surface, and I'll just draw them like this because the scale is too small for me to actually draw any kind of structure for you, but you can think of them as floating on the surface like little ships, and this is -- these are called surfactant molecules.

Q. Surfactant?

A. Surfactant. It's very much like soap. Soap is a -- soap is a surfactant.

The reason soap works the way it does, the reason it can remove dirt and oily material is because if I take one of these and schematically blow it up, these little blue molecules look like this with this being the gas and this being the film, the fluid film, and it has these two little tails that stick out. So they're represented here. So here you have these little molecules floating along here. And the reason soap works is because this part of the molecule likes to be in a water kind of phase, it's hydrophilic, it likes water, and this part doesn't like water, so you see it's trying to get away, and

it orients itself so that it's facing out toward the gas phase. So when you wash your hands or you wash your clothes with these kinds of molecules, this part of it, the hydrophilic, allows you to dissolve the molecule in your wash water, and this part of the molecule, which likes the more oily kind of materials, attaches to what you might call the dirt, and then sequesters it, and then once it's sequestered, you hope that your washing machine goes through the drain cycle rather than spin cycle; otherwise, it gets filtered all back on your clothes again. And then it's taken out with the drain water and you put in new water and you continue this rinsing process until you've washed all of these out.

Now the reason that these are in the lung is because they help the lung, these alveoli, to keep their shape. It keeps these alveoli from collapsing. Because obviously if they -- there's only air on the

inside, they're like little balloons, and if they collapse, that would also be drastic in terms of our ability to exchange oxygen and CO2.

In fact one of the real problems that premature kids have is sometimes they're born before they've had a chance to manufacture enough of this surfactant, and so they have respiratory distress

syndrome, and one of the ways that physicians actually treat that is to instill surfactant molecules into the child's lungs to help them inflate their little alveolar sacks so that they can breathe until they're able to make enough of this on their own.

So a molecule which is trying to cross from the gas phase into the blood phase has to encounter quite a few interesting structures, the surfactant layer, this hypophase, the cells, basement membrane, this cell wall, the interior of this cell, and this cell wall, and finally into the blood.

So this is the structure that represents the little gas exchange units in the -- in the lung, and if we can just sort of keep this scale in mind, it has that sort of egg-shell thinness to it.

Q. Doctor, let me ask you: When oxygen -- when we breathe in, are there charged and uncharged molecules? What -- what takes place in the alveoli --

A. Well in --

Q. -- during this exchange of gases?

A. With oxygen, oxygen is a -- just the oxygen gas molecule O2, and it will pass through this structure -- while it looks formidable, if the gas

concentration is high on this side and low on this side, the structure is thin enough to be able to transport the metabolic amount of oxygen we require in order to survive, given the amount of oxygen that's in the atmosphere, the pressure of the oxygen in the atmosphere, and the lack of oxygen on this side.

Another way of looking at it is people who climb high mountains, like Mount Everest, you hear about how they struggle to breathe and they have to use oxygen. Well this is because when you get high enough in our atmosphere the oxygen concentration begins to drop, the pressure of oxygen begins to drop is another way of looking at that, and therefore when you breathe in, you don't breathe in sufficient oxygen to have a concentration high enough to push the required amount into the blood and you begin to get into oxygen deprivation. And you feel this coming. I -- I am a private airplane pilot, and sometimes if you go generally above 12 or 13 or 14 thousand feet and you don't have supplemental oxygen, you will feel that, you can feel the -- the lack of oxygen affecting you, and it's just because there's

not enough driving force to push the oxygen you require into the blood.

Now what about other kinds of molecules that you might -- that might be transported across this structure? And let me just draw a schematic molecule that may be trying to get through.

Actually, let me cross that out. An actual molecule that might be trying to get through here would be sort of like -- not even that big, really, really tiny. I wouldn't even be able to draw it here that you'd be able to see it. If you give me -- I don't want to confuse you and make you think that molecules are this big, they're not. Really, really tiny, so -- on this scale. So let me come over here apart from this and draw a little molecule and just -- I'll just treat it as a little box.

Now what enables this molecule to get through this membrane? What -- what characteristics work in its favor and what characteristics work against it? It's well known in biology that if this molecule is more oil soluble; that is, hydrophobic, like these little tails, it will have a little greater propensity to traverse this biological membrane than if it has the tendency to be very water soluble. So oil solubility helps. And one of the reasons is is because many of the structures that the molecule has to cross have oil type of characteristics, such as

these membranes. Albeit, it also has to move through some spaces that look like it has more water, but on balance, the more oil-soluble materials will travel through a biological membrane more rapidly.

Likewise, molecules that carry a charge; that is, if this carries a positive charge or it carries a negative charge, charged particle -- and molecules can carry charges. They can, depending on their electron balance -- an electron gives it a negative charge. A molecule can be neutral, have no net charge plus or minus like a battery, or it can be positively charged or it can be negatively charged.

Charged molecules tend not to go through biological membranes nearly as easily and readily as uncharged. So what we're looking for in terms of the ease of transport is a general rule of thumb that hydrophobic molecules and uncharged molecules have the best opportunity to get through the most rapidly as opposed to a hydrophobic or a water-loving molecule that carries a charge.

Q. Thank you, doctor.

MR. CIRESI: Your Honor, we'd offer Exhibits 25011 and 25012 for illustrative purposes.

MR. BERNICK: No objection, Your Honor.

THE COURT: The court will receive 25011

and 25012.

MR. CIRESI: Does Your Honor want to continue at this point, or should we take --

THE COURT: Maybe we should recess for lunch. Reconvene at 1:30.

(Recess taken.)

AFTERNOON SESSION.

THE CLERK: All rise. Court is again in session.

(Jury enters the courtroom.)

THE CLERK: Please be seated.

THE COURT: Counsel.

MR. CIRESI: Thank you, Your Honor.

MR. CIRESI: Good afternoon.

(Collective "Good morning.")

BY MR. CIRESI:

Q. Good afternoon, doctor.

A. Good afternoon.

Q. Could you direct your attention back to Exhibit 12408, which is the April 14th, 1972 memorandum by Dr. Teague of RJR, and specifically, if you could look at page four once more.

At page four, at the end of the paragraph which is continued over from page three, Dr. Teague is talking about work that should be done with regard to knowledge about nicotine absorption, action, elimination, enhancement, et cetera.

Did your review of the defendants' documents lead you to the conclusion that the defendants did investigate those various aspects of nicotine?

A. Yes, they certainly investigated the

physiological effects of nicotine and were particularly concerned about means whereby rate of absorption of nicotine could be enhanced, in particular by altering the form of nicotine, as that

would allow them to develop a system. And I -- what I mean by the system, the entire delivery system, so that under those circumstances it would effectively be more efficacious or efficient for the transfer of nicotine into the human body.
Q. And was one of those means by which they enhanced nicotine was the free nicotine or pH form?
A. Yes. They spent a great deal of effort examining means whereby the form of nicotine could be altered by altering the acidity or basicity, and that's what Mr. Ciresi meant by its pH.
Q. And does nicotine need to be in a free base form to transfer through the alveolar membrane?
MR. BERNICK: Your Honor, this is leading, again, in form.
THE COURT: It is leading.
MR. BERNICK: Object to form.
THE COURT: It is leading, counsel.
BY MR. CIRESI:
Q. What if any form does nicotine need to be in to transfer through the alveolar membrane?

A. Well certainly the preferential form is -- is an uncharged form of the molecule, as I explained earlier, as opposed to a charged form of the molecule, and the free base form of nicotine is the uncharged form.
Q. Doctor, before we get into that, I'd like to explore with you some of the defendants' documents with respect to nicotine as a drug. Can you direct your attention to Exhibit 11361, which again is in volume one of the books in front of you.
Is this one of the documents that you reviewed with respect to forming your opinions in this case?
A. Yes, it is.
Q. And did you find this document to be representative of the documents that you reviewed with regard to the subject matter of nicotine as a drug?
A. Yes, I did. There was a great deal of consistency throughout in the documents I reviewed.
Q. This is a BATCo document, confidential BATCo document entitled "BRAINSTORMING II" dated April 11th, 1980.
MR. CIRESI: Your Honor, we would offer Exhibit 11361.
MR. BERNICK: No objection, Your Honor.

THE COURT: Court will receive 11361.
BY MR. CIRESI:
Q. Can you direct your attention, then, doctor, to the -- first of all, the title, which is --
Before we do that, let's go up to the upper left -- right-hand corner. This is a document that bears the initials of ALH, which is a Mr. Heard from BATCo, and if we turn to the second page, you'll see in the distribution column that Mr. Heard was an R&D

executive, was one of the individuals to whom this document was distributed, and also a Dr. Greig, whose documents we've already seen. And the author of this document was a Mr. Crellin, C-r-e-l-l-i-n, R&D technical specialist for BATCo.

If you'd direct your attention back to the first page then. First of all, if we look at paragraph two on the first page, "Drug Diversification," "In a world of increasing government intervention, B.A.T should learn to look at itself as a drug company rather than as a tobacco company."

Now were terms like that found by you in the defendants' documents?

A. Yes, they were.

Q. And if you'd look at the first paragraph, it talks about a chemically engineered cigarette. Did

you find terms like that in the defendants' documents?

A. Yes, I did.

Q. And what did you come to conclude, if anything, with regard to what was meant by "chemically engineered cigarettes," doctor?

A. That the cigarette is -- is viewed as a -- as an engineered device for the specific purpose of delivering nicotine in a particular fashion to the human body, and by that I mean it has its various components which have to be brought together, have to be assembled and have to be quality controlled.

In this particular case, what they're talking about is a cigarette-like device, but one that accomplishes the same effect, and that of -- of delivering nicotine. And under "Drug Diversification," they're basically saying if we're a drug company, then should we consider other drugs other than nicotine, perhaps, in the future.

This is a brainstorming session talking about what the industry might look like at the end of this century. But this is a -- this is pharmaceutical company talking to us.

Q. Can you direct your attention, then, doctor, to Exhibit 10602, which is in the same volume. This is

a B.A.T. Company Ltd. document dated May 3rd, 1974, it's addressed to all members of a conference, has an agenda for the conference, and is signed by A. D. McCormick, who is the secretary of the company.

Is this one of the documents that you reviewed in the course of your investigation into this matter?

A. Yes, it is.

Q. And was this document consistent with the other documents that you found of the defendants during the course of your investigation?

A. Yes, it's consistent.

Q. And does the document form part of the basis of your opinion in this case?

A. Yes, it does.

MR. CIRESI: Your Honor, we'd offer Exhibit 10602.

MR. BERNICK: Your Honor, we object to at least portions of the document. There is handwriting --

We know it's produced from our files, but there's handwriting not identified in the document, and the document pertains to a whole variety of subjects that we don't believe there's been a foundation laid through this witness that he has the expertise to address. So if there's a particular

portion of the document that's going to be addressed, I might be able to simply agree to the testimony -- or the document coming in for that purpose, but right now the tender is too broad.

THE COURT: Whose writings are on the document, counsel?

MR. CIRESI: Employees of B.A.T, Your Honor.

THE COURT: Is it -- did the document --

Was it received by the plaintiffs in this form?

MR. CIRESI: That's correct, Your Honor.

THE COURT: The court will receive 10602.

BY MR. CIRESI:

Q. Can you first put up the first page. All right.

There we see the author, Mr. McCormick, attaching the revised agenda for the conference. Could you turn -- direct your attention to page 588, and by that I'm referring to the last three Bates numbers, doctor. Now this sets, across the front -- or the top three columns, "ASSUMPTIONS, POLICIES," and "GUIDELINES." The upper left-hand corner we see "STRICTLY CONFIDENTIAL," and the title of this document is "SMOKING AND HEALTH." And there's a guideline over on the right-hand side which is directed to all group companies.

Based on your review of the B.A.T and B&W documents, would B&W be one of the group companies of B.A.T?

A. Yes, that's my understanding.

Q. And what is set forth in the guidelines here, doctor?

A. Well the guidelines seem to follow from a series of assumptions that have been made, a series of policies that have been proposed, and then a series of guidelines which are structured in such a way as to set forth action items based upon the assumptions in the -- in the policies --

MR. BERNICK: Your Honor --

Q. -- and direct --

MR. BERNICK: Excuse me. I would move to strike the answer. I don't believe a foundation has been laid that this witness has a factual basis for knowing how the guidelines were promulgated or what was done with them. All we have is the document.

THE COURT: Okay. The answer will stand.
BY MR. CIRESI:
Q. In the note to the guidelines it states, "The following guidelines are set out for those Group Companies which already having to deal with the smoking and health issue. It is obviously not

suggested that in those countries, where the issue is not yet a live one, companies should bring it to the fore by initiating action, but they should nevertheless prepare themselves to act on the guidelines, as appropriate, if and when the issue does become a live one."
Now under the guideline columns, I'd like to direct your attention to Bates number 592, and specifically to number six under "GUIDELINES." What is set forth in that guideline, doctor, with regard to tobacco as a drug?
A. Well, put this in context again. You'll remember that this is a confidential document dealing with smoking and -- and health, and one of the issues that is of concern here is the potential that governments will wish to control activities of the tobacco industry by legislation. And with specific reference to the issue of drugs it notes that if tobacco were to be placed under a Food and Drug law, classification of tobacco under the food section would be acceptable, but classification of tobacco as a drug, as a drug, should be avoided at all costs.
These -- these people, while they recognize nicotine as a drug, are concerned that they may be regulated as an industry because they in fact deliver

a drug, and they don't want that to happen.
Q. Were there --
THE COURT: Counsel.
MR. CIRESI: I'm sorry.
MR. BERNICK: I have a motion, Your Honor. My motion is to strike the last answer of the witness and to lodge a continuing objection. These questions pertain to regulatory policy and legislation. I don't believe that the witness has been established as having expertise in the area. Moreover, his last answer purported to speak to the intent of the people involved in this communication. I don't believe that that is an issue for the expert to address, and I believe that's an issue for the jury to address.
THE COURT: The answer will stand.
BY MR. CIRESI:
Q. During the course of your review of the documents, did you ascertain what if anything the defendants attempted to do with regard to having tobacco regulated as a drug?
MR. BERNICK: Your Honor, can I have a continuing objection along the lines of my prior motion to this line of questioning?
THE COURT: Yes, you may.

MR. BERNICK: Thank you.

THE COURT: As -- as to this exhibit.
A. I'm sorry, could you repeat that?
Q. Sure. I --
Were there other documents of the defendants that indicated the same type of attitude as is --
A. Yes.
Q. -- as is expressed here?
A. Definitely. They were very concerned about the possibility of imposed legislation that would control their industry and regulate their product as a drug.
Q. And was there also reference here in the guidelines section of this document with regard to threshold levels of nicotine?
A. Yes. There was -- there is on page 96 in the Bates number.
Q. Okay, last two numbers, 96. Is that at the end of that page, doctor?
A. It's under "GUIDELINES" again, item -- item iii. It says, "We should resist, as far as possible, the imposition by Government of maximum levels for tar and nicotine. If a Government is determined to take such action, we should strive to have the levels fixed sufficiently high to cover the majority of brands on the market. If necessary, we should point out that a reduction of nicotine below a level

satisfactory to the consumer might lead to increased per capita consumption."
Q. Now --
A. And --
Q. I'm sorry, go ahead, doctor.
A. And the essence of this is a -- a concern that if there is government regulation and if some limit were to be set on the maximum level of tar and nicotine, it could be set at a level below which certain brands were already in the marketplace, which would narrow this dose-range window in which the industry could operate relative to what I was saying earlier this morning about the drug dose-range window.
The notion that, if necessary, we should point out that a reduction of nicotine below a level satisfactory to the consumer might lead to increased -- increased per capita consumption speaks to the fact that if they're forced to pull the roof down on the dose window, then the cigarettes that are now available will not deliver the dose above that window any longer, and that leaves in jeopardy consumers that were used to smoking cigarettes of a higher tar -- higher tar and nicotine level, in which case they'll point out that smokers will smoke more

cigarettes -- this is a form of what's known as compensation -- to make up for the lack of nicotine delivery in the lower tar and nicotine cigarettes that would be forced upon them because of government regulation.

Q. Can you direct your attention now, doctor, to Exhibit 10539, which is in evidence. This is a memo from Mr. Dunn, other memos of which the jury has seen authored by Mr. Dunn, to Dr. Wakeham, dated February 19th, 1969, referring to Jett's money offer. And Jett was Jett Lincoln, who was the vice-president of finance for Philip Morris at this time.

Is there reference in this document with respect to Philip Morris's opinion as to whether or not nicotine was a drug?

A. Yes. If you'll look at the -- I believe it would be the third paragraph beginning with, "I would...," states, "I would be more cautious in using the pharmic-medical model -- do we really want to tout cigarette smoke as a drug? It is, of course, but there are dangerous FDA implications to having such conceptualization go beyond these walls."

Q. Now doctor, in the last paragraph is made the following statement: "More broadly, the focus of his proposed research effort expansion should be, in my

opinion, less upon the improvement of the product and more upon the psychophysiological entity responding to the product."

Can you describe what that means from a chemical standpoint?

A. What it means to me is that he's suggesting that rather than spending effort improving in some manner the product itself, which would be the cigarette and the delivery system that's associated with the cigarette, one ought to be spending more time on the psychophysiological entity that could be interpreted as being either the human brain -- the human being or the brain or the place where the drug is having this activity, so that if you had a better idea of what the response mechanism was, then ultimately you could drive that back into product improvement if you chose to. But he's basically saying spend your time there rather than improving the product, at least in this memo.

Q. Now doctor, based on your review of the documents, did Philip Morris and RJR, B.A.T, B&W and Lorillard, reflect continuous research and development into nicotine during the 1960s?

MR. BERNICK: Your Honor, this is a -- this is leading again in form. Object on grounds of form.

THE COURT: It is leading.

BY MR. CIRESI:

Q. What did your review of the documents reflect with regard to whether those companies researched nicotine during the '60s?

A. They were aware in the 1960s of the product that they were producing, that it was a drug-delivery product for nicotine, and of course in their research laboratories, efforts were spent on examining just that issue.
Q. What did your review reflect, if anything, with respect to research into that area or subject matter in the 1970s?
A. It continued. It continued into the 1970s and 1980s and it continues at least to the last -- the most recent documents I've seen.
Q. Can you direct your attention now, doctor, to Exhibit 10255 --
Before we get to the document, let me ask you this: Based on your review of the defendants' documents, what were you able to ascertain that the defendants considered to be their primary product?
A. There was no question --
MR. BERNICK: Excuse me. I have an objection, Your Honor.

THE COURT: Go ahead.
MR. BERNICK: It's an extremely broad question. It covers all defendants. It's not been tied down to any particular document. So I object to the breadth of the question and the lack of foundation.
THE COURT: I think your question should be rephrased, counsel.
BY MR. CIRESI:
Q. Were the documents consistent among the defendants with respect to what product they considered to be their primary product?
MR. BERNICK: Your Honor, I object again. This has been rephrased, and now it's leading as well.
THE COURT: I'll let the answer stand -- the question stand.
A. There's no question -- there's --
There's no issue there. The -- the product -- the product was nicotine.
Q. Can you direct your attention now to Exhibit 10255, which is a Philip Morris document dated August 12th, 1980, marked "PERSONAL & CONFIDENTIAL" from Mr. Osdene, director of research, to Dr. R. B. Seligman and directors, with carbon copies to a Mr. Sanders

and a Mr. Kuhn.
Is this one of the documents that you reviewed which forms the basis of your opinions in this case?
A. Yes, it is.
Q. Is it consistent with the other documents that you reviewed regarding this subject matter?
A. Yes.
MR. CIRESI: We would offer, Your Honor, Exhibit 10255.
MR. BERNICK: No objection, Your Honor.

THE COURT: The court will receive 10255.
BY MR. CIRESI:
Q. Now Mr. Osdene, the director of research for Philip Morris, addressed the nicotine program in paragraph five. "This program includes both behavioral effects as well as chemical investigation. My reason for this high priority is that I believe the thing we sell most is nicotine."
Was that statement consistent or inconsistent with other Philip Morris documents that you reviewed?
A. It was consistent.
Q. Was it consistent or inconsistent with respect to the documents of the other defendants that you reviewed?
A. It was consistent across the board.

Q. Can you direct your attention up to number two where Mr. Osdene is stating the following: "Biological Effects of Smoke."
"In view of the clouds on the horizon, we must be more aware of the activities of additives, materials, et cetera."
Now doctor, when a company designs and places in the stream of commerce a drug-delivery device, are they required to do research into the effects of the device with regard to good practices of design, based upon your experience?
MR. BERNICK: Your Honor, I -- I don't believe that the witness has been tendered, neither in his expert report or otherwise, as an expert in FDA regulation of drug-delivery devices, and on those grounds we'd object to this line of examination.
THE COURT: I don't recall that the question asked him about FDA requirements.
MR. CIRESI: It did not, Your Honor.
THE COURT: You may answer the question.
A. Certainly in the course of developing a drug-delivery device, certainly the ones that I've been involved with, we're terribly concerned about whatever materials we put into the -- into the device that may in turn be taken in by the recipient, if

it's more than just the drug itself; for instance, an adjuvant or another additive or a solubilizer, which are sometimes put into drug-delivery systems. And we're very careful to be sure that to enable the device to perform in a more efficacious -- efficacious way, that we don't bring harm to the recipient by having done so.
Q. Doctor, can you direct your attention, then, to Exhibit 13165, which is an RJR document, and that would be in volume two.
THE COURT: Say it again, counsel.
MR. CIRESI: 13165, volume two.
BY MR. CIRESI:
Q. Is this another document that you had reviewed and does it form part of the basis of your opinion in

this case?
A. Yes, it does.
Q. With respect to the issue of nicotine as a primary product, is it consistent with the documents that you reviewed of not only RJR, but the other defendants in this case?
A. Yes.
MR. CIRESI: Your Honor, we would offer Exhibit 13165.
MR. BERNICK: No objection.

THE COURT: Court will receive 13165.
BY MR. CIRESI:
Q. First of all, the title is a little -- there we go -- "REST PROGRAM REVIEW, May 3, 1991." What did REST stand for, doctor?
A. I believe it stood for Re-Establishment of Solubles in Tobacco.
Q. What's a soluble?
A. Well in this case it's the water-soluble extracts that can be removed from -- from tobacco by a method of processing. The idea here was at some point, then, to add them back in a selective way. It was a large program that was being conducted at RJR in this time period.
Q. Doctor, can you turn your -- to the next page, which is Bates number 9575, which is stamped "CONFIDENTIAL" and it's entitled "REST PROGRAM REVIEW, May 3, 1991." This is the overview. And is there a reference there to "Controlled Nicotine Process Development and Engineering?"
A. Yes, it's one of the headings on that page.
Q. Now the REST program, was this particular program, to your knowledge, initiated by RJR?
A. Not to my knowledge.
Q. Can you direct your attention to exhibit 9584 of

this exhibit. This is entitled "Controlled Nicotine Process." I'd like to specifically ask you to look at the "Basis" section of this document.
"We are basically in the nicotine business. It is in the best long term interest for RJR to be able to control and effectively utilize every pound of nicotine we purchase. Effective control of nicotine in our products should equate to a significant product performance and cost advantage."
With regard to the references to RJR being in the nicotine business, is that consistent with what you found in its documents for the time period 1950s up to 1994?
A. Yes, it's very consistent.
Q. Was it consistent with what you found in the other defendants' documents?
A. Yes, it was.
Q. Can you direct your attention, then, to Exhibit 18089 in the same volume, which is an admitted exhibit. This is a document in January of 1972

marked "CONFIDENTIAL," entitled "MOTIVES AND INCENTIVES IN CIGARETTE SMOKING," it's written by William L. Dunn, Jr. of Philip Morris Research Center, Richmond, Virginia, and it references a conference that was held an island in the Antilles.

Is this one of the documents that you reviewed in the course of your investigation in this matter?
A. Yes, it is.
Q. And with respect to the subject matter of nicotine and nicotine as the primary product of the defendants, is it consistent with the documents that you reviewed?
A. Yes.
Q. And does it form part of the basis of your opinion?
A. Yes, it does.
Q. Can you turn to page five of that document. On this page does Mr. Dunn refer to what the product of the industry is, and does he describe a drug-delivery device, being the cigarette?
A. Yes, he does, beginning at the second paragraph.
Q. Can you explain what that is, doctor, and tell us what you learned from this document with regard to Philip Morris.
A. Well he states clearly, "The cigarette should be conceived not as a product but as a package," and "The product is nicotine." So that's -- that's evident. Then he goes on to talk about how a cigarette is but one of many package layers. "There is a carton, which contains the pack, which contains

the cigarette, which contains the smoke." And "The smoke is the final package." Because of course that's where the nicotine is being delivered. "The smoker must strip off all these package layers to get to that which he seeks."

He goes on to say, "But consider for a moment what 200 years of trial and error in designing has brought in the way of nicotine packaging," and now we're talking about the system as a whole.

"Think of the cigarette pack as a storage container for a day's supply of nicotine.

"It is unobtrusively portable." That's an advantage to it.

"Its contents are instantly accessible.

"Think of the cigarette as a dispenser for a dose unit of nicotine."

And when I see terms like that, "dose unit of nicotine," I, of course, think of it in terms of a drug-dispensing device.

"It is readily prepped for dispensing," in this case, the drug "nicotine."

"Its rate of combustion meters the dispensing rate, setting an upper safe limit for a substance that can be toxics in large doses."
Q. Let me stop you there. What does that mean,

"its rate of consumption meters the dispensing rate?"
A. Basically there is going to be an upper limit to how rapidly the combustion process can occur, and that is responsible for the distillation of the nicotine into the smoke, so there's going to be a limit on basically how the user can access the drug that's in the reservoir, and this would then prevent the recipient from reaching this upper-level threshold maximum of toxicity, since, of course, this is an extremely toxic chemical.
Q. Can you turn over to the next page, then, please.
A. Then he goes on to say, "Think of a puff of smoke as the vehicle of nicotine.

"A convenient 35 cc," that means 35 cubic centimeters, that's a volume. "A convenient 35 cc mouthful contains approximately the right amount of nicotine." So here he's talking about have we delivered enough in a -- in a -- in a particular time or a particular, in this case, puff.

"The smoker has wide latitude in further calibration." This I find very interesting from a drug-delivery device point of view. We talk about puff volume, which is how much you take in, the puff interval, which is how frequently you puff, the depth

and the duration of inhalation, meaning how deeply you inhale and how long the smoke is in contact with the tissues.

"We have recorded wide variability in intake among smokers. Among a group of pack-a-day smokers, some will take in less than the average half-pack smoker, some will take in more than the average two-pack-a-day smoker." And what this is referring to is that one aspect of a cigarette that distinguishes it from most other drug-delivery devices which are, in a sense calibrated at the factory, and now a drug to be released over a specific period of time is preset and it's not something that the recipient has control over, but with a cigarette, by virtue of the way in which it's smoked, there is now built into it this biological feedback mechanism that I told you about earlier, so they can regulate while smoking the drug intake.
Q. How does Mr. Dunn, who's known as The Nicotine Kid at Philip Morris, conclude this portion of his report?

MR. BERNICK: I object to the form of the question and the characterization of Mr. Dunn.

MR. CIRESI: I'll rephrase it.

THE COURT: Rephrase it, please.

BY MR. CIRESI:

Q. How does Mr. Dunn conclude this portion of his report?
A. He says, "Smoke is beyond question the most optimized vehicle of nicotine and the cigarette the most optimized dispenser of smoke." So he's basically saying that it would be very difficult to think up a better way to deliver nicotine to the human body.
Q. And was that expression of Mr. Dunn's one that you found in other of the defendants' documents?
A. Yes. Equivalent thoughts were expressed in the other defendants' documents.
Q. Can you direct your attention now, doctor, to Exhibit 11283, which is back in volume one. This is a document dated August 28th, 1979, written by the managing director of R&D, Mr. Blackman, it references a meeting which took place with a Mr. P. L. Short, who was the marketing manager, on the 22nd of August of 1979, it's entitled "KEY AREAS - PRODUCT INNOVATION OVER THE NEXT 10 YEARS FOR LONG TERM DEVELOPMENT."
Is this one of the documents that you reviewed?
A. Yes.
Q. And with respect to the issues of nicotine, is

it consistent with the other documents that you reviewed of the defendants?
A. Yes, it is.
Q. Does this document form part of the basis of your opinion?
A. It does.
MR. CIRESI: Your Honor, we'd offer Exhibit 11283.
MR. BERNICK: No objection.
THE COURT: The court will receive 11283.
BY MR. CIRESI:
Q. Does this document refer to nicotine and its role in cigarettes in the opinion of B.A.T?
A. Yes, it does. It -- that in fact is the theme of the document.
Q. Can you direct your attention, please, to page three of this document, and specifically number three which is stated as one of a set of assumptions.
"We are searching explicitly for a socially acceptable addictive product involving:
"a pattern of repeated consumption.
"a product which is likely to involve repeated handling.
"the essential constituent is most likely to be nicotine or a 'direct' substitute for it."

Doctor, in the course of your review of the defendants' documents, including B.A.T, was there continuing research in looking at how nicotine could be conveyed to the consumer?
A. Yes. That's one of the primary underpinnings of all their activities.

Q. And in this document, did Mr. Blackman, the managing director of research and development, also talk about the typical development path for a smoker?
A. Yes, he did.
Q. And is that set forth on page one of the document?
A. Yes, it is. It begins on page one.
Q. Direct your attention to page one.
A. It's at the bottom.
Q. And does he set forth basically three stages for the smoker going from curiosity, parents, image/peers in the first stage, to a second stage of acknowledgment of pleasure and perceived benefits, and then into a third stage of dependence?
A. That's how it's described, yes.
Q. And were there, in your review of the documents of the defendants, other references to nicotine as the dominant product in the stage of smoking by smokers in getting that product?

A. Yes. I saw repeated reference to the issue of how it is people begin to smoke and then stay engaged in smoking, because they realize that if you haven't developed a craving for nicotine or have never had it, then why would you start to begin with? And so the documents that -- that I have -- have reviewed and that I have seen discuss this in some sense a paradox or a dilemma of attracting the user before the user understands why -- what will come next. What will come next, of course, afterwards is the second and third stages, finally dependence on a smoking habit. But the key is how to get them started, and there's somewhat of a dilemma or a paradox there, and that was described in a number of the documents that I -- that I reviewed.
Q. And were these documents --
MR. BERNICK: Excuse me. I have a motion. Move to strike, Your Honor. I believe the witness is now getting into a area of testimony in which he has not been qualified as an expert, which is the reasons for smoking and smoking behavior. He's been qualified as a chemical engineer, and I believe that exceeds the scope of his qualifications and his expert report.
MR. CIRESI: We're not going into the

motivations, Your Honor. We're dealing only with the drug, the pharmacological effects. We're not getting into addiction or dependence.
MR. BERNICK: That's why I moved to strike the prior answer.
THE COURT: Well the prior answer will stand, but as long as we aren't going into it.
BY MR. CIRESI:
Q. Doctor, were there consistent documents that addressed the pharmacological effect of the drug in the documents you reviewed?

A. Yes. There were many documents discussing pharmacological effect of -- of nicotine as a drug. No question about that.
Q. All right. Can you direct your attention now to the Brown & Williamson document, Exhibit 13873. It would be in volume two.
This is Exhibit 13873, it's dated February 28th, 1990, it is marked "RESTRICTED," it's entitled "Chemosensory Research" by R. R. Baker, manager of R&D. Has a B&W stamp at the top.
Is this one of the documents that you reviewed?
A. Yes, it is.
Q. Does it form part of the basis of your opinion?
A. Yes, it does.

Q. Is it consistent with the other documents that you reviewed of the defendants which dealt with the product of the tobacco industry?
A. Yes.
MR. CIRESI: Your Honor, we'd offer Exhibit 13873.
MR. BERNICK: Your Honor, I believe this was an incomplete document. There's another plaintiffs' exhibit that I believe is a more complete version of this document. It's 12087. We don't object to the introduction of 12087; it's the more-complete version.
MR. CIRESI: This document was produced in this fashion by the defendants. It goes from page one through the final page, with Mr. Baker's name at the bottom -- at the end.
MR. BERNICK: Your Honor, we --
MR. CIRESI: If there's another document that they wish to introduce later, Your Honor, I believe they should do that.
MR. BERNICK: We produced many, many, many, many copies of the same document as required by the court's orders. The complete version was also produced. It has a page three which I don't believe is in the one that's currently being tendered.

We've brought 12087 to the court here, which is one of the plaintiffs' own exhibits, and all we're suggesting is the complete document be used rather than the incomplete document.
MR. CIRESI: Your Honor, at the end of --
We're not going to use page three. If they wish to do it, we can just attach it to this document.
MR. BERNICK: Well I'd object --
THE COURT: Why don't -- why don't we use the whole document.
MR. CIRESI: Well we will get a copy and introduce it, then, at the end -- at the break.
THE COURT: Okay. Do you have a copy available?
MR. BERNICK: Yes, it's right here.
THE COURT: Why don't we use that, counsel.

MR. CIRESI: We'd offer Exhibit 12087.
MR. BERNICK: No objection.
THE COURT: The court will receive 12087.
BY MR. CIRESI:
Q. Now doctor, you're looking at what's in your book as 13873, but I'm going to deal with the first page, which is the same.
Does Mr. Baker in the introduction deal with the ultimate product of the tobacco industry?

A. Yes, he indicates that the ultimate product of the tobacco industry is nicotine.
Q. And does he indicate in there that B&W will be researching development of low tar/medium nicotine cigarette smoke?
A. Yes, that's what he goes on to say. Actually the "research should -- should continue," implying that it's been going on, "to be directed at the development of low tar/medium nicotine cigarette smoke." It points out that "Nicotine alone in smoke isn't practical, nor are extreme tar-to-nicotine ratios, since nicotine is too irritating," and because of that, "other substances are required for sensoric reasons." Which basically is another way of saying that since nicotine, which is the drug you want to deliver, is -- can be very irritating, you're going to have to add other components to the delivery device to make it acceptable so that you can get it into the human being and get it into the lungs and get it absorbed and get it to the brain.
Q. And did your review of the defendants' documents reflect whether or not that type of research continued over the time period 1950s into the 1990s?
MR. BERNICK: Objection to form. Chemosensory research, or some other particular kind

of research?
THE COURT: Can you clarify that question, please?
MR. CIRESI: Sure.
Q. Research into nicotine and its relationship to other components of the cigarette.
MR. BERNICK: I object to the form. I'm not sure what's being asked.
THE COURT: Okay. You may answer that question.
A. Yes. Over the years, all the defendants conducted research into means whereby nicotine could be efficiently delivered by this device and in a means that would put it, as it's been referred to, as an attractive dosage form. The problem is that the drug doesn't taste good. And it's not unlike trying to give our kids medicine that tastes bad. What do you do to it? You put additives in it, you put tastes or flavors in it so that it becomes palatable to take the drug that's being delivered. It's not unlike what is being said here.

Q. Doctor, can you direct your attention to the next exhibit in the book, which is Exhibit 13878, which is a Brown & Williamson document in 1971 written by R. R. Johnson, who's the marketing

committee secretary, reflecting a meeting that was held on June 30th of 1971 to discuss past research on nicotine. The individuals in attendance at that meeting were Sir Charles Ellis, Drs. Green, Felton, Wood, Ayers, Backhurst, Cinkotai, Evelyn, Hilburn and Johnson, and two other gentlemen by the names of Nicholl and Dymond, D-y-m-o-n-d.

Is this one of the documents that you reviewed?

A. Yes, it is.

Q. And does it form part of the basis of your opinion?

A. It does.

Q. Is it consistent with the other documents of the defendants that you reviewed with respect to the reference into nicotine by the defendants during the course of time from 1950 to the 1990s?

A. Yes.

MR. CIRESI: Your Honor, we'd offer Exhibit 13878.

MR. BERNICK: Your Honor, 13878 begins -- first page is page ten and the second page is page eleven. Exhibit 2948, Plaintiffs' Exhibit 2948 we believe to be a complete copy of the document with pages one through nine. So we'd propose that, as before, if Mr. Ciresi wants to use 2948, which is

a complete copy of the document, that we have no objection to that.

MR. CIRESI: Your Honor, these documents were produced in this fashion. Many of them were taken apart. And no objection was made to this document pursuant to the orders of the court. If counsel has objections to these documents, the procedure is set up so that they would do that before we get into the courtroom like this.

THE COURT: Did you --

MR. BERNICK: Your Honor --

THE COURT: Excuse me, counsel. Did you receive 13878 as in the form of page ten and page eleven?

MR. CIRESI: We did, Your Honor.

THE COURT: All right. So that the first nine pages were not received?

MR. CIRESI: Not with this document, they were not. This document was received as is with two Bates numbers consecutive. The Bates numbers are, the last four, 2257 and 2258.

THE COURT: What's the Bates number for page nine?

MR. BERNICK: The Bates number for page nine out of the whole document is 500012136.

THE COURT: So it was not received in order.
MR. CIRESI: It was not, Your Honor.
THE COURT: All right.
MR. CIRESI: And therein lies the problem.
THE COURT: All right. The objection is overruled then. We'll receive pages ten and eleven as Exhibit 13878.
MR. BERNICK: So Your Honor's clear on the record, I was giving you the Bates number out of the full document. A second document was produced as page ten and eleven as we had it in our files. I understand the court has ruled, but I want to make sure --
THE COURT: Okay.
MR. BERNICK: -- that the record is clear.
THE COURT: All right. Thank you.
BY MR. CIRESI:
Q. This document is entitled "Comments on Nicotine," and at the outset, a meeting is referenced that was held on June 30th and it also references those that were in attendance.
I'd like to direct your attention, sir, to the paragraph right after the list of the individuals who were in attendance at the meeting.

"The meeting -- The purpose of the meeting was to discuss the results from Projects MAD HATTER and HIPPO, and to stimulate further discussion on the importance of nicotine to the industry."
First of all, MAD HATTER, what does that refer to?
A. Well obviously it refers to a code name they used for this project having to do with studying the -- the desirable and undesirable components of smoke and also to inquire as to what the body does with -- with nicotine. It's --
The Mad Hatter, as some of us might remember, was the infamous little rabbit in the Alice in Wonderland story, and I guess he was nuts because in the 16th and 17th centuries and earlier when hatters made hats, they used mercury in rendering the felt, and mercury was a neuropoison, and so I guess it was common that people who made hats were nuts.
MR. BERNICK: Your Honor, I object, I believe that's objectionable under Rule 403. There's no relevance. It's outside the scope of this case.
THE COURT: No, I -- the answer will stand.
BY MR. CIRESI:
Q. This meeting involved nicotine; correct, doctor, as referenced in this document?

A. Well it was a meeting that was to -- to discuss past research on nicotine, so these folks were

gathering together to talk about what it was they had been doing in these major efforts, the MAD HATTER effort and the Project HIPPO effort that was being conducted at that time.
Q. And does the document reflect what Sir Charles Ellis said with respect to what business the tobacco industry is in?
A. Apparently he started the meeting by saying, as it says in the document, that he's -- he's, of course, being paraphrased here by the author of this document. It says "Sir Charles started the meeting by saying that he had first brought out the concept that we are in a nicotine rather than a tobacco industry." This, again, being consistent with similar statements and expressions made in a number of documents.
Q. And if you move down a couple paragraphs -- well let's -- let's go to the next one.
Does it reference there what Project MAD HATTER was originally arranged to maximize?
A. Yes. I tried to summarize when you asked me what the MAD HATTER meant. It was to maximize the desirable constituents of smoke and minimize the

undesirable ones. That was first part of it. The second part was to find out what the body does with nicotine.
Q. And in the third paragraph, is there reference to what happens to nicotine in the bloodstream?
A. Unless --
Are you talking about paragraph three?
Q. I guess it would actually be four, if you take the first one, "A meeting...." It says, "Although nicotine in the bloodstream is...."
A. Okay. I was looking at the wrong paragraph. Sorry.
In the paragraph beginning with "Dr. Evelyn," it says, "Although nicotine in the bloodstream is rapidly metabolized, some is apparently stored for a much longer time in places where it can become involved in the stress biochemistry."
Q. And what is "metabolized," doctor?
A. "Metabolized" is -- refers to the disassembly of the molecule by the body. If you want to think about the molecule I draw -- drew for you earlier, it's taking -- taking it apart and as the whole part of the body biochemistry molecules that we take into our body are assembled and they're disassembled, and that's what we mean by metabolism.

Q. And if you direct your attention to the next paragraph, is there reference there to the phenomenon that you just discussed or the attribute of nicotine of its odor or irritation?
A. Well here they're talking about a particular form of nicotine known as free nicotine, sometimes referred to as free base nicotine. And it's the form

of nicotine which is uncharged, so it's neutral species. And he says, "Another easy test of free nicotine odor and irritation involves smelling some as it is eluted from a gas chromatograph - a small amount will almost knock one over and the aroma is apparent." So it -- it has a very pungent and acrid odor. Very unpleasant smelling.

Q. Can you describe, doctor, just briefly, what -- what is "eluted from a gas chromatograph?"

A. A gas chromatograph is a -- an analytical instrument that is used to take a -- a mixture of chemicals that are in the vapor phase or are put into the vapor phase and then separates them one by one by one. So if I have a mixture of, let's say, four chemicals in a -- in a gas, typically we use gas chromatography to learn what they are by injecting this gas mixture into the device, and then the response of the device is to provide us with

separated fractions of each of the components which then can either be further analyzed or even identified by virtue of how long it took them to go through the -- through the instrument.

So if you're trying to -- if you have, in this case, free base nicotine in a -- in a -- and it would be in a vapor environment, and you wanted to identify or measure how much was there, you would -- you could use this kind of a instrument.

Q. Directing your attention, then, to the next page, is there a reference there to other investigation that was going to be conducted with regard to pH of whole smoke on a puff-by-puff basis?

A. Refers to a Dr. J. D. Backhurst indicating that he's setting up an analysis for pH of whole smoke on a puff-by-puff basis. PH, again, referring to the relative acidity or basicity of -- of, in this case, smoke. And they point out that it correlates with his previous interest in extractable nicotine, which refers to a -- an analytical means whereby one can identify nicotine in its uncharged form by making measurements in solutions.

Q. Doctor, can you turn now to Exhibit 10227, which is a Philip Morris document dated January 10th, 1978 from the director of research, Mr. Osdene, to the

files, with copies to Mr. Goldsmith, who was the president of the company, to Dr. Wakeham, who was a senior scientist, to Mr. Seligman, who's the vice-president of R&D, and two other individuals, Mr. Holtzman and Mr. McDowell.

Is this one of the documents that you reviewed during the course of your investigation?

A. Yes, it is.

Q. And did this document form part of basis of your opinion?

A. Yes, it did.

Q. And with respect to the defendants'

investigation and research into nicotine, was it consistent with what you found in the other defendants' documents?
A. Yes.
MR. CIRESI: We'd offer Exhibit 10227.
MR. BERNICK: No objection, Your Honor.
THE COURT: The court will receive 10227.
BY MR. CIRESI:
Q. You see that this refers to a CTR meeting in New York City, January 5th, 1978, and Mr. Osdene reports that "At Mr. Goldsmith's," who's the president's, "request, Dr. Seligman, Mr. Holtzman and I met with Dr. Gardner, Dr. Hockett and Mr. Hoyt at the CTR

offices in New York," the object being "to review contracts carried out by Microbiological Associates."
I'd like to direct your attention to the last paragraph which reads as follows with regard to these contracts: "Dr. Seligman brought up the grant by Dr. Abood in which one of the stated aims was to make a clinically acceptable antagonist to nicotine. This goal would have the potential of putting the tobacco manufacturers out of business."
What is an antagonist to nicotine?
A. Well an antagonist to nicotine would be another molecule which would have the tendency to bind at the same receptor sites in the brain that nicotine would bind at. And so if you gave somebody an antagonist to nicotine and the antagonist bound to the biological receptors in the brain and filled up all the receptor spots, sort of like cars filling up a parking lot, then when the nicotine would come along there would be no place for it to go, so it wouldn't exert its biological effect. So that would be an antagonist to nicotine.
Q. Now you testified, doctor, that nicotine was pharmacologically active?
A. Yes, I did.
Q. Did your review of the defendants' documents

reveal whether or not the scientists and researchers of the defendants agreed that nicotine was pharmacologically active?
A. Yes, they agreed to that.
Q. Okay. Can you direct your attention to Exhibit 12270, which is in volume one. It is an RJR document. Is that one of the documents that you reviewed?
A. Yes, it is.
Q. It's dated September 21, 1976, the subject is "Product Characterization, Definitions and Implications," it's to a Mr. A. P. Ritchy from John L. McKenzie.
Does this document form part of the basis of your opinion?
A. It does.
Q. Was it consistent with other of the documents

that you reviewed of the defendants?
A. Yes.
MR. CIRESI: Your Honor, we'd -- we'd offer Exhibit 12270.
MR. BERNICK: No objection.
THE COURT: Court will receive 12270.
BY MR. CIRESI:
Q. First of all, on the first page there's a

definition of terms.
A. Yes.
Q. And how is nicotine defined in this RJR document?
A. States that "Nicotine is the pharmacologically active alkaloid ingredient in tobacco smoke, and is collected on a special filter during the smoking procedure. The nicotine is reported separately from other smoke components."
So it points out that nicotine is indeed pharmacologically active.
Q. And can you turn to page two in this document, which is discussing the cigarette products characterization, definitions and implications, and specifically with regard to nicotine, what is reported there?
A. It refers to it as a psychopharmacological agent, "The psychopharmacological agent in tobacco, which is one of the key factors in satisfaction," that's the nicotine. Goes on, "Although the issue is not decided, current theory advocates that a smoker will consume enough cigarettes to reach his satisfaction level." So they're talking about getting up into this dose range where it exerts its pharmacologic activity. "However, should the

nicotine be too low, the smoker will become fatigued with smoking before achieving satiation." Meaning that if the smoker is smoking a -- a delivery device that's delivering an inadequate amount, and since the smoking process involves inhaling and sucking, that it could frustrate the smoker if in fact the product that the smoker is smoking is unable to deliver the appropriate dose. "On the other hand, too much nicotine in the smoke will make the product so strong that the consumer is unable to enjoy the product." And we've seen that if nicotine is delivered in such a way that it exerts adverse effects, either by irritation or taste, that that would be a negative. It goes on to say, "Typical nicotine in smoke values for cigarettes range from 0.2 milligrams to 1.8 milligram per cigarette." And this would refer to the number of milligrams of nicotine that are taken in by the -- by the recipient. So you can see that there is a -- there is a range as one would expect.
Q. And does the author of this memorandum, a Mr. McKenzie, also address the issue of tar and its characterizations -- characteristics in the

cigarette?
A. Yes, he does.
Q. And what is reported with respect to tar,

doctor?
A. Well he points out that "The designation tar is a misnomer for the complicated but discrete mixture of solid and liquid materials in smoke aerosol excluding water, which is omitted, and nicotine, which is reported separately."

And I should point out that cigarette smoke is -- is an aerosol. It's little droplets suspended in a vapor or a gas phase much like fog. And when you see smoke, what you're seeing is light scattered off of these little particles; the same reason that clouds are white and that you can see fog when you see fog and so forth.

Now these particles, these little liquid particles contain all the material that was released when the cigarette was -- was burned, and then the vapor phase surrounding them contain some other materials, some are the same, some are different.

What is done here is to basically take the little liquid droplet and divide it into three little bags. One is the water that's in the droplet, and then of the -- depending on which internal document one chooses to look at, anywhere from five thousand to three million chemical components that are in this little liquid drop after you take the water out. You

pull one of them out, nicotine, you measure it, and then the other thousands, tens of thousands of chemicals that remain is called tar.

So tar is not a molecule, it's not a -- an identifiable pure chemical compound. It is a -- it is an uncharacterized mixture of the whole suite of chemicals, some of which have been identified, in fact many of which, some thousands of which have been identified, and many thousands of which have not.

In chemical engineering, tar is basically what is the stuff that's left over after you refine crude oil and is sitting at the bottom of the number one distillation column. And it's usually sold out to -- if you can't make anything more with it, it's sold out and sold as asphalt and put on roads or something like that. It, too, is a very uncharacterized material, which is, presumably, where the name "tar" came from. But it's very, very important to remember that -- that tar is a -- is an uncharacterized substanc and it is not a pure material at all.

So you can see how this -- this industry has focused on the one material, nicotine, and that is the one molecule that they pull out of this huge collection of other uncharacterized molecules -- as I said, some have been measured -- and focus on it. So

when you think of cigarette smoke the way the industry thinks of it and the way they typically report it is tar, nicotine, and then the water, which is then removed.

Now they say "The smoke tar contains the majority of smoke materials responsible for the taste of cigarette smoke." So we've learned that nicotine in and of itself is irritating and has an acrid, pungent odor and is basically unpleasant. "A reduction in tar leads perforce to reduction in taste perception." So if you are removing tar, say, by filtration in a cigarette, then some of the taste will be depleted. "Application of more top flavor materials and selection of stronger flavored tobaccos are typical procedures for amelioration of the loss of taste associated with tar reduction." And what that means is in the cigarette manufacturing process, flavors are added to the nicotine in order to give it certain taste and aroma characteristics that might have been lost while you were trying to reduce the tar delivery of the cigarette.

Q. Now doctor, there's also a section of this document by Mr. McKenzie which relates to pH, and I'd like to direct your attention to the last paragraph on page two where he states as follows: "The pH also

relates to the immediacy of the nicotine impact. As the pH increases, the nicotine changes in its chemical form so that it is more rapidly absorbed by the body and more quickly gives a "kick" to the smoker. However, if the pH becomes too high the smoke cannot be inhaled as is the case with cigar smoke."

Now without getting, at this point, too deep into pH and free nicotine, was the investigation of pH a subject matter that was investigated by not only RJR but the other defendants in this lawsuit as reflected by their documents?

A. Yes, definitely. It was pervasive throughout the documents.

Q. And if you turn to the last page, it states, "Overall a cigarette is a complex chemical reaction chamber for the generation of an aerosol containing flavoring materials and nicotine. The variables affecting the smoke constituents are highly interdependent and smoker satisfaction is best maintained by a controlled balance of many factors."

Now I want to just focus, if we could, on that last phrase, "smoker satisfaction is best maintained by a controlled balance of many factors." In the engineering of a cigarette, does the term "recipe"

have any connotation?

A. Well -- well it can, sure. It would have to do with the manner in which the various elements or

constituents of what is put into a cigarette are brought together in terms of types and amounts, just like making a cake or a pie or something like that. We call them specifications.
Q. And did you, during the course of your investigation, review formula documents which have been characterized as Category II documents?
A. Yes. The formula or specification documents were the documents that were kept locked in the two rooms in the Minneapolis law offices.
Q. Can you direct your attention now, doctor, to Exhibit 13668, which is in volume two. This is a B.A.T and B&W document marked "CONFIDENTIAL," dated April 7th, 1982, it's directed to W. L. Telling, Brown & Williamson International Tobacco in Louisville, Kentucky, from G. O. Brooks of British-American Tobacco Company, Ltd., a member of the B.A.T Industries Group, and it attaches a paper number 16 entitled "HUMAN SMOKING BEHAVIOR."
Is this one of the documents that you reviewed during the course of your investigation?
A. Yes, it is.

Q. Does it form part of the basis of your opinion?
A. It does.
Q. And with respect to nicotine as a pharmacologically active ingredient in cigarettes, is it consistent with the other documents of the other defendants that you reviewed?
A. Yes.
MR. CIRESI: Your Honor, we'd offer Exhibit 13668.
MR. BERNICK: No objection, Your Honor.
THE COURT: The court will receive 13668.
BY MR. CIRESI:
Q. First if we can take a look at the cover letter to Mr. Telling from Mr. Brooks dated April 7th, 1982, and referencing the smoker compensation study. If we turn to the next page, a study, which is marked "CONFIDENTIAL," is entitled "PAPER 16 - HUMAN SMOKING BEHAVIOR."
Could you direct your attention, please, to page five of that document.
MR. BERNICK: Your Honor, it occurs to me, in the context of Mr. Ciresi's remarks just before this document, there was a reference to Category II and the lock and key documents.
THE COURT: Yes.

MR. BERNICK: I don't know that there's a suggestion -- I don't know if it was intentional or not -- that this somehow was a Category II document. If there was not, I think that should be made clear.
THE COURT: Maybe -- maybe --
MR. CIRESI: Isn't --
THE COURT: Maybe you should clarify it for the jury.

MR. CIRESI: This one is not a Category II.
THE COURT: All right.
MR. CIRESI: That question was asked with reference to the recipe business on the last document we were looking at.
THE COURT: All right. Just so the jury understands that. This is not a Category II document.
BY MR. CIRESI:
Q. Can you go to page five of this document. And the number I'm using now is at the top. I'm not using the Bates number. The last three Bates numbers are 615. I'd like to direct your attention to the last paragraph. In this document B&W and B.A.T state, "Nicotine is the most pharmacologically active constituent in tobacco smoke and is probably the most usual factor responsible for the maintenance of the

smoking habit."
Now with regard to the reference to nicotine as the most pharmacologically active constituent, is that consistent with what you saw in other documents, sir?
A. Yes, it is.
Q. And in the paragraph immediately above there is a reference to impact and the amount of smoke that gives satisfaction in smoking, then a reference to "This is a similar mechanism to Pavlov's dogs." Do you see that?
A. Yes, I do.
Q. What's being referenced there, doctor?
A. Well what they're talking about is when people smoke, what -- what do they experience? What sorts of sensations, irritations? What might they smell? What -- and they also talk about -- impact is something -- something else, and as I understand, impact has to do with a sensation that occurs in the back of the throat, and I've heard it described as a sensation that occurs in the upper chest when people smoke and inhale, and that these taste or sensory perceptions are -- are felt immediately upon taking in the -- the puff. Now that puff will be inhaled, and within a few seconds, seven to ten seconds,

something of that order, those nicotine molecules will be embedding themselves in the receptors in the brain.
The reference to Pavlov's dogs, then, is that when you take this smoke into the oral cavity and nasal cavity and you experience these sensations, even though they might be irritating to some -- to some extent, you've developed an association from that experience to know that a reward is coming, and the reward that soon comes, within seconds, is the reward that occurs when the nicotine attaches itself to the cholinergic receptors in the brain. And the relationship to Pavlov's dogs was the -- the

experiment there was Pavlov would feed his dogs, and while the dogs were being fed he'd ring a bell, and then each time he'd feed the dogs, again he'd ring the bell. And it showed that the dogs would develop an association with eating and hearing the bell rung, and the way he proved that is he would bring the dogs in, he'd ring the bell but there would be no food, and the dogs would begin to salivate. And so this is a conditioned response, an association between one experience and then generally a reward experience that follows.

Q. Doctor, can you direct your attention to Exhibit

105 -- I'm sorry, 11089. 11089. That's in book one. That's an admitted document.

Again, can you direct your attention on that document, "COMPENSATION FOR CHANGED DELIVERY," to page five, and is there a reference there with respect to nicotine's pharmacological effects?

A. Yes. In the beginning of the -- the only -- the -- the first paragraph on that page, the first indented paragraph beginning "When..." says, "When smoke is inhaled by the smoker nearly all the nicotine is transferred from the smoke in the lungs to the bloodstream. This transfer to the blood is very rapid and nicotine is circulated to all parts of the body within seconds. Nicotine has pharmacological effects both in the brain and other parts of the body."

Q. Now again, doctor, were statements to that effect made by the other defendants in other documents of those defendants?

A. Yes, they were.

Q. Can you direct your attention to Exhibit 10523, which is in volume one.

Do you have it, doctor?

A. Yup.

Q. And this is a Philip Morris memo written by Mr.

Charles, who is the manager of the biochemistry group and later became vice-president for research, to Dr. Osdene, who at that time was director of research, and is dated February 23rd, 1982.

Is this one of the documents that you've reviewed in this case?

A. Yes, it is.

Q. Is it a document that forms part of basis of your opinion?

A. Yes.

Q. And with respect to the subject matter of nicotine as pharmacologically active, does it -- is it consistent with other documents that you've reviewed of the defendants?

A. Yes.

MR. CIRESI: We'd offer Exhibit 10523, Your Honor.

MR. BERNICK: No objection.

THE COURT: Court will receive 10523.
BY MR. CIRESI:
Q. Doctor, I want to read the introduction and then go to certain facts that Mr. Charles is suggesting that Philip Morris should address. First of all, the title of this document is "Comments on 'Future Strategies for the Changing Cigarette,' National

Conference on Smoking and Health."
And I'll try to read the words. I know it's difficult to -- to see those on the overhead.
"On February 22nd, 1982 (the day of the 1982 Surgeon General's press conference on Smoking and Health) you asked me to review the subject document and provide you with comments. The comments below are those of a concerned employee with a 22" -- or "a 20-year association with Philip Morris R&D, of which the past ten years have been directly involved with smoking and health research. I consider myself well trained in the biological and chemical sciences and qualified to make the following comments which should be taken as constructive criticism with suggestions as to how to approach the solution to some of the problems."
And then if you go to the last page -- I'm sorry, the second-to-the-last page, page four, "The quote, Future Strategies, end of quote, document" --
Could we go to the top of that, please? Thank you.
"The, quote, Future Strategies, end of quote, document is even more disturbing than the Surgeon General's comment. Terms such as - standard setting, government or voluntary agency guidelines,

qualitative analysis of tar, emphasis on brands with very low yields, disclosure of additives, regulation of future additives - are all worthy of concern. Again, this reflects a continuing pressure on the industry and requires a strategic response.
"Let's face the facts:
"Cigarette smoke" -- number one, "Cigarette smoke is biologically active.
"A. Nicotine is a potent pharmacological agent. Every toxicologist, physiologist, medical doctor and most chemists know that. It's not a secret."
And over on to the next page, I, "We do not know enough about the biological activity of additives which have been in use for a number of years."
Was the opinion stated by Mr. Charles in this memorandum representative of statements you found in other of the defendants' documents over the years that you examined them?
A. Yes.
Q. Could you find any documents which stated that nicotine was not pharmacologically active?
A. No.
Q. Doctor, you talked about a dose range required

for a drug to have its pharmacological effect; correct?

A. Yes.
Q. Based on your review of the defendants' documents, was there a rough dose range for cigarettes as measured by the FTC measurements?
A. Yes. An approximate dose range can be delineated from measurements that have been made on commercial cigarettes.
Q. And what was that dose range?
A. I would place it approximately in the range of deliveries of .1 milligram to upwards of 1.4 milligrams of nicotine.
Q. And did the defendants, based on your review of the documents, investigate this dose range?
A. Yes, intensively.
Q. What if any concern did they express about the dose range going too low, below a threshold?
A. Well when they -- when they began to drop the tar levels in cigarettes, since I indicated to you that nicotine is one of the many thousands of constituents of tar, it also, too, began to drop. So lowering the tar levels in cigarettes, as occurred over the last few decades, well the nicotine levels began to drop, and as that took place I could see in the documents as time went on a growing concern of wanting to be sure that the nicotine levels could be

maintained in such a way as they didn't fall through the bottom of the dose-range threshold, because if they did, as we've seen, there would be no business left because they're in the business of delivering nicotine for its pharmacological activity. And so this gave rise to a great deal of internal research in their laboratories to determine methods whereby, as the tar levels were dropping, the nicotine levels could be maintained in such a way as not to have them drop below this dose-range window, which also involved a search, if you will, for what that dose-range bottom is, where it would lie.
Q. Doctor, can you direct your attention, then, to Exhibit 10392, which is in volume one of the books in front of you. This is a 1959 B.A.T document. See it down at the bottom?
A. Yes, it is.
Q. And this is one of the documents that you reviewed?
A. Yes, it is.
Q. Does it form part of the basis for your opinion?
A. Yes.
Q. Is it addressed to the issue of dose range?
A. Yes, it is.
Q. Is it consistent with the documents of the

defendants that you reviewed in this case?
A. Yes, it's consistent.
MR. CIRESI: Your Honor, we'd offer Exhibit 10392.
MR. BERNICK: No objection, Your Honor.
THE COURT: Court will receive 10392.
BY MR. CIRESI:
Q. The document is entitled "COMPLEXITY OF THE P.A.5.A. MACHINE AND VARIABLES POOL," and at the bottom you'll see a research and development stamp with the date August 26, 1959.
If you could, doctor, would you turn to page three -- and that's at the top. That's the Bates number, last three pages, 117. And I'd like to direct your attention to the portion of the document on that page which is entitled "Considerations."
Is the dose-range issue addressed in that section of this document?
A. Yes, it's -- it's addressed in this section under "Considerations" when the -- it's stated that "On the question of nicotine and its effect on the smoker there can be two extreme forms of approach," the first, "Keep up the nicotine content of cigarettes in order to maintain the, as yet, firmly entrenched nicotine habit developed by the majority

of smokers." And two, "Reduce the nicotine per cigarette as much as possible and thus satisfy the trend of consumer demand as it is today." So these are the two extreme choices.
Goes on to say, "To follow No. (1)" -- which is to keep up the content -- "To follow No. (1) above too closely would be to deprive oneself of the chance of participating in the still (on a worldwide basis) increasing demand for less nicotine." However, alternative two, "To follow No. (2) too closely might end in destroying the nicotine habit in a large number of consumers and prevent it ever being acquired by new smokers. True, deprived of an increasing amount of nicotine per cigarette, consumers may tend to smoke more cigarettes, but this can only go on up to a point."
And so what they're saying is that if we keep the nicotine levels where they are, we'll miss what they perceive to be a growing market for lower nicotine levels. They would like to be in that market as well. But if you reduce it too much and people go there, it could end up destroying the nicotine habit that they have, or worse yet, be unable to attract new smokers to engage in the habit because now you're below the threshold of activity.

Q. And do they then express an opinion that they should attempt to seek an optimum amount?
A. So having said that, and realizing that these are the two extremes, as one might expect, you don't

gravitate it to either extreme necessarily, but you try to find something that is, if you would, a compromise or happy medium. So "Somewhere between the above two extremes there surely must be an optimum offer to consumers and it is this point -- which will no doubt vary from country to country and from time to time -- that we should try to find and adhere to. Fortunately, the search need only be single-ended as there is no need to seek means for giving consumers more nicotine per cigarette than can today be made available to them."

So the notion is that there's something that lies in between these two extremes that's optimal, and that's where we should position ourselves.

Q. And can you direct your attention to another B.A.T document, which is 13668 --

THE COURT: Counsel, I think we should take a short recess at this time.

MR. CIRESI: Fine, Your Honor.

THE CLERK: Court stands in recess.

(Recess taken.)

THE CLERK: All rise.

(Jury enters the courtroom.)

THE CLERK: Court is again in session.

Please be seated.

BY MR. CIRESI:

Q. Doctor, in your review of the documents, did the defendants also express concern that their profits were tied to their product nicotine?

A. Yes, they -- they did make that point.

Q. Can you direct your attention back to Exhibit 11283, which is in volume one, which shows it's a B.A.T. Company Ltd. document written by Mr. Blackman, the managing director of R&D?

A. Yes.

Q. And on page four, to the second full paragraph, quote, "We also think that consideration should be given to the hypothesis that the high profits additionally associated with the tobacco industry are directly related to the fact that the consumer is dependent upon the product."

Now the product being referred to was nicotine, doctor?

A. Yes, that's correct.

Q. Can you direct your attention now to Exhibit 13668, which we have already reviewed, it's "HUMAN

SMOKING BEHAVIOR," a B.A.T document. It's in volume two. And again, I'd like to address your attention to the subject matter of whether the nicotine level gets too low.

Can you turn -- direct your attention to page ten of that document. Is there expressed on that page a concern about the threshold level between just acceptable and rejection?

A. At the very bottom of the page, the last two

sentences states, "If delivery levels are reduced too quickly or eventually to a level that is so low that the nicotine is below the threshold of pharmacological activity then it is possible that the smoking habit would be rejected by a large number of smokers. It is not known where this threshold between just acceptable and rejection lies."
Q. Was that concern expressed by other of the defendants based on your review of their documents?
A. Yes. They understood the existence of this lower threshold, they understood the consequences of moving through that lower threshold with regard to their business being in the industry of delivering nicotine to the consumer. So that it in fact is pharmacologically active implies that it has to be above the threshold; if it's not, there simply

wouldn't be a product, wouldn't be a business.
Q. Can you direct your attention, then, to Exhibit 12777, which is an R. J. Reynolds document related to this issue, and it's dated 5-24-71.
Is this one of the documents that you reviewed during your investigation into this matter?
A. Yes, it is.
Q. Is it --
Does it form part of basis for your opinion?
A. Yes.
Q. And is it consistent with others of the defendants' documents that you reviewed on the issue of the threshold level of nicotine in cigarettes?
A. Yes.
MR. CIRESI: Your Honor, we would offer Exhibit 12777.
MR. BERNICK: No objection, Your Honor.
THE COURT: Court will receive 12777.
BY MR. CIRESI:
Q. This is a memorandum from A. H. Laurene, L-a-u-r-e-n-e, the manager of the Chemical Division, to the director of research, Dr. Murray Senkus, S-e-n-k-u-s, and I'd like to direct your attention to number four, "Habituating level of nicotine, paren, How low can we go?"

Now doctor, what is being referred to there?
A. Well they're talking about possible projects with an off-site contractor, and one of the undertakings that's listed is trying to determine what is this lower threshold, what is its value and how can we establish it. And the threshold they're talking about is the threshold that they will pass through, and if they do, the nicotine will no longer be habituating. So it's a very clear distinction, at least in my mind and I believe in their minds as well, that this threshold exists, and that they are moving toward it and they need to establish what it is so that they can level the nicotine dosage off, because they know they just can't pass through it.

Q. Can you direct your attention to subparagraph two which is, "Absorption of nicotine in mouth versus lungs, paren, blood levels, urine levels."
What type of research is being referred to there, doctor?
A. Well the nicotine is taken in in a puff into the mouth and then down into the -- through the tracheo-bronchial system and then into the lower reaches of the respiratory system and the lungs. It's possible that it can be taken up into the body beginning in the mouth and then through the upper respiratory

tract down into the lungs, and it appears that they are interested in learning about the extent to which nicotine is absorbed in the mouth versus the lungs, and they're proposing, for instance, to measure blood levels or urine levels of nicotine as some kind of indicator as to those processes.
Q. Can you direct your attention to Exhibit 10170, which is in the same volume, and this is a Lorillard document directed to the same subject of threshold levels. It is a memorandum authored by the vice-president of marketing to the president. The vice-president of marketing is R. -- Richard E. Smith, to the president, Mr. Ave, A-v-e, to a J. G. Flinn, F-l-i-n-n, and finally to Dr. A. W. Spears, who had become the future CEO of the company. It's dated February 13th, 1980, it's stamped "SECRET."
Is this one of the documents that you reviewed?
A. It is.
Q. And does it form part of the basis of your opinion in this case?
A. It does.
MR. CIRESI: Your Honor, we would offer Exhibit 10170.
MR. BERNICK: No objection, Your Honor.
THE COURT: Court will receive 10170.

BY MR. CIRESI:
Q. Do you see the author, Mr. Smith, and who it's directed to, in fact it's a Lorillard memorandum marked "SECRET," dated February 13th, 1980.
In the first part of this memorandum, up to where it says "Discussion Points," is the issue of the threshold level addressed by Lorillard in 1980?
A. Yes, it is, under the heading "Goal," the goal there is to "Determine the minimum level of nicotine that will allow continued smoking," essentially what we heard just in the previous document.
"We hypothesize that below some very low nicotine level, diminished physiological satisfaction cannot be compensated for by psycological satisfaction. At this point smokers will quit, or return to higher tar and nicotine brands."
Q. And did you review Philip Morris memoranda that related to the same issue of the threshold level of nicotine?

A. Yes.
Q. Can you direct your attention to Exhibit 11171 in volume one. I'm sorry, I misspoke, 11771.
Is this one of the documents you reviewed during the course of your investigation?
A. Yes.

Q. And does it form part of the basis for your opinion?
A. It does.
Q. This is a document dated November 8th, 1990, Philip Morris U.S.A. interoffice correspondence to the director of research, C. K. Ellis, E-l-l-i-s, from Frank Gullotta, G-u-l-l-o-t-t-a, C. S. Hayes, H-a-y-e-s, and B. R. Martin.
MR. CIRESI: We would offer, Your Honor, Exhibit 11771.
MR. BERNICK: No objection, Your Honor.
THE COURT: Court will receive 11771.
BY MR. CIRESI:
Q. And can you direct your attention to paragraphs three and four. At that point in this memorandum, is Mr. Gullotta addressing the issue of the dose range?
A. Yes, he is. He's -- he's reviewing the -- the work that has been accomplished in electrophysiological studies to Philip Morris U.S.A., and at the third point he says, "We have shown that there are optimal cigarette nicotine deliveries for producing the most favorable physiological and behavioral responses." And so in his research and in the work that's conducted at that laboratory, he

claims that they ascertained the optimal nicotine deliveries which would render the most favorable physiologic and behavioral response. And he also goes on to say that the laboratory demonstrated that all forms of nicotine are not behaviorally or physiologically equal and points out that this observation is important for evaluating research cigarettes where the addition of nicotine is -- is necessary, implying that if you are going to do research for cigarettes to which you've added nicotine, you have to be cognizant of the form of nicotine that you add to them because all are not equal in terms of their physiologic responses.
Q. And doctor, my French isn't very good, but under the subject it says "Raison d'etre;" is that correct?
A. "Raison d'etre."
Q. And what does that mean?
A. The reason to be.
Q. Can you direct your attention to Exhibit 10856, which is in the same volume.
A. Say again.
Q. 10856.
This is another Brown & Williamson Tobacco Corporation document dated September 13th, 1963.

It's authored by the director of research, R. B. Griffith, and it's directed to a chemist, Mr. John Kirwan of British-American Tobacco Company Ltd., and it has carbon copies going to Sir Charles Ellis, senior research individual at BATCo, Mr. T. M. Wade, Jr., vice-president of research, and Mr. Finch, F-i-n-c-h, who became president of Brown & Williamson.

Is this another document that you reviewed in the course of your investigation?

A. Yes, it is.

Q. And is it --

Does it form part of the basis of your opinion?

A. It does.

Q. And does it deal with the subject matter that we've been discussing, and that is, the nicotine levels in cigarettes with regard to the threshold levels?

A. Yes.

MR. CIRESI: Your Honor, we would offer Exhibit 10856.

MR. BERNICK: No objection, Your Honor.

THE COURT: Court will receive 10856.

BY MR. CIRESI:

Q. First of all, you see the title page, you see Mr. Kirwan's name and the date. If you look down to

the bottom of that page, is there a reference to nicotine and its importance with respect to smoker response?

A. Yes, in the -- under heading number one, it says that "Nicotine is by far the most characteristic single constituent in tobacco and the known physiological effects are positively correlated with smoker response."

Q. Now if you go over to page two, you had reference earlier, doctor, in your testimony to the recipe nature of the business with regard to the engineering of cigarettes. Is that concept referenced at the top of this page?

A. Yes, it's discussed.

Q. And what is the import of what's being discussed in that memorandum at that point?

A. Well in this particular case, as we've discussed, the reservoir for nicotine is -- is the tobacco product that's contained in the nicotine rod, and it has to be delivered to the recipient in a palatable way. So that the device would be used, and what they're discussing is the importance of adding sugars in the blending operations to enhance the smoker acceptance. So sugar is a -- is an additive that is put into cigarettes to make them more

palatable. It's part of the -- part of the blend recipe.
Q. Is sugar a --
When combusted, is sugar a base or an acid?
A. Well when it's -- when it's combusted, it -- it's -- it changes its chemical form and typically the degradation products will be acidic.
Q. Did your review of the defendants' documents indicate whether or not that was taken into account by the defendants with regard to the levels of nicotine or pH as it may affect nicotine in blending cigarettes?
MR. BERNICK: Objection to form, leading.
THE COURT: It is leading.
Q. What if any effect did the documents show sugar had on blending?
A. Well there will be certain taste characteristics that are imparted by the decomposition products of the sugars and also by the chemical reactions that the sugars undergo during the decomposition process, and to the extent that some of those decomposition products are acidic, then it will tend to have an effect on what is known as smoke pH, it will have an effect of tending to reduce it somewhat. And this just goes into the balance of the total cigarette

design, the extent to which you want to control pH and the extent to which you want to control taste. Sometimes additives work in synergistic ways and sometimes they give you a -- a dual result, a good result or a bad result, and this all has to be weighed in in the compromise that results in the design of the cigarette.
Q. Is that referenced in the first full paragraph after the indented paragraph which is numbered two?
A. That's where he's talking "It is doubtful if any experienced tobacco blender would question seriously the conclusion that nicotine and sugar are important, but things become a bit more difficult when one considers the question of desirable or optimum levels for either nicotine or sugar or a balance between the two."
And then that question in turn becomes more complicated when you realize that the recipient is going to have variations in personal preference. There may be health issues associated with that question, the influence of other constituents, the accustomed use, what someone's used to, and possible influences of either climatic variables on consumer's acceptance. So there are many, many variables that enter into this overall design of the cigarette.

Q. In this document, does Mr. Griffith, the director of research, point out that the nicotine level of B&W's cigarettes was not obtained by accident?
A. Yes, he does.

Q. Direct your attention to the bottom of page three.
A. Yes, he says -- he's discussing the levels of nicotine in not only B&W cigarettes, but competitive cigarettes as well, and he points out that "Certainly the nicotine level of B&W cigarettes given in the above table was not obtained by accident." In other words, it was determined or it was deterministic. "It may be well to remind you, however, that we have a research program in progress to obtain, by genetic means, any level of nicotine desired."
Q. And if you turn over to the next page, does he also reference the -- in the last paragraph the recipe nature of the engineering of a cigarette?
A. Well he actually does it in a -- in a couple of places. On the fifth line he says, "I think that we can say even now that we can regulate, fairly precisely, the nicotine and sugar levels to almost any desired level management might require. Of this I am confident."

Then he goes on to say, "It should be recognized that nicotine and sugar levels are not the only things important in determining smoking quality. It should be emphasized that these are but two constituents in a very complex tobacco leaf and that there are other materials in the leaf which must affect smoking quality. I am certain that when these have been identified, ways can be found to control their level just as we can control nicotine and sugar levels and we will some day achieve the goal of precision manufacture." The notion therefore being is that the ultimate -- a day will come when there will be perhaps a time that you can fully prescribe the constituent makeup of this drug-delivery device, and from a -- certainly from a manufacturing point of view in terms of controlling the output, that would be desirable if that could in fact be achieved.
Q. Doctor, can you direct your attention now to Exhibit 11386. It's in the same volume.
This is a B.A.T. Company Ltd. document which is dated March 29th, 1976 and is entitled "THE PRODUCT IN THE EARLY '80S."
Is this one of the documents that you reviewed in this litigation and does it form a part of the basis of your opinion?

A. Yes, it does.
Q. Is it consistent with respect to the subject matter of other documents that you've reviewed regarding other defendants in this case?
A. Yes.
MR. CIRESI: Your Honor, we would offer Exhibit 11386.
MR. BERNICK: Your Honor, we have no objection to the exhibit coming into evidence.
THE COURT: Court will receive 11386.

BY MR. CIRESI:
Q. Can you direct your attention to page two of that document, and specifically the paragraph which is numbered five. Is there reference therein to the concept of the threshold level of nicotine and the defendants' concern about finding the right levels?
A. At the very end of that paragraph it's stated that "Nicotine is an important aspect of, quote, satisfaction, unquote, and if the nicotine delivery is reduced below a threshold, quote, satisfaction, unquote, level, then surely smokers will question more readily why they are indulging in an expensive habit."
Q. In the beginning of that paragraph, does -- is there a reference to the danger in the current trend

of lower and lower cigarette deliveries?
A. Well they point out in "Taking a long-term view, there is a danger in the current trend of lower and lower cigarette deliveries -- that is, the smoker will be weaned away from the habit."
Q. And apart from nicotine, now, is there -- does the author also address whether or not a reduction in tar would be of any concern?
A. He states that "The reduction in tar deliveries is not -- is not of critical concern and, providing the pressure on the market is sufficient to cause an, quote, across-brands, unquote, tar reduction, opportunities are opened up in the market for a low-tar-with-taste cigarette." So there's an issue of the threshold dose level being maintained for nicotine, not so for tar.
Q. In this memorandum, does the author reference the cigarette designs which might offer an image of health reassurance?
A. Yes, he does.
Q. Can you direct your attention to page six, and specifically paragraph 14.
A. Yes, I have it.
Q. "Looking further down the road, the possibility exists that, as inhalation tests are developed and

accepted, then filters might offer a selective means of controlling smoke toxicity. Well before that date, however, opportunities exist for filter and cigarette designs which offer the image of 'health re-assurance'."
This document was authored in 1976. Did you see other documents of the defendants which referenced health-reassurance cigarettes?
A. Yes, I've seen reference to that.
Q. Can you direct your attention, then, doctor, to page three of this document, and I'm looking at the paragraph (d), "Alternative plant products." Does this research memo also talk about the issue of other types of narcotic plants and the augmentation of cigarettes with other substances?

A. Yes. They refer to the fact that there are some 80 species of plants which contain hallucinogens, stimulants, inebriants and hypnotics, and there is some discussion about whether other plants might replace tobacco, with tobacco being the one plant that provides the drug nicotine. Points out that the only material which has received a lot of attention is marijuana, and the controversy on whether or not to legalize soft drugs is frequently aired. "In the last two years the public debate appears to have

receded -- one cynical explanation," however "is that the habit has now extended to include, quote, the establishment, end quote, or upper-classes. In the illicit use of marijuana, relatively large doses of active principal are involved." They go on to say, "If the use of such drugs was legalized, one avenue for exploitation," that is for the industry, "would be the augmentation of cigarettes with near sub-liminal levels of the drug."

Q. Let me ask you something there, doctor. Does this evidence to you an indication on the part of the author that the cigarette industry was really considered a drug industry by these individuals?

MR. BERNICK: Objection to the argumentative form. It's leading.

THE COURT: It is leading, counsel.

MR. CIRESI: I'll withdraw the question, restate it.

BY MR. CIRESI:

Q. What if anything does this signify to you, doctor?

A. Well it clearly points out that the person writing this, and -- and the company that this person represents, believes that they are indeed in a drug-delivery business, in a -- in a business to

provide drugs to the consumer, the primary drug and the only drug at the present time being nicotine, but their eyes are open to other possibilities or to adding additional drugs to the delivery device they already have. I think that's quite consistent with this notion to which the defendants agree; that is, that they are in the drug-delivery business and that drugs are their products.

Q. Can you direct your attention now to Exhibit 11259. This is a B.A.T. Company Ltd. confidential document dated 16th of February 1983 regarding notes of a meeting of tobacco company and research directors, there was Dr. L.C.F. Blackman from B.A.T, who was the managing director of R&D, and also Dr. M. Bourlas of Philip Morris.

Is this one of the documents that you've reviewed?

A. Yes.

Q. Does it form part of the basis of your opinion?

A. It does.

Q. And this document was written by Dr. Blackman on the 18th of February, 1983, and he sent copies to a number of individuals, including Mr. Ely, Mr. Dickson, Mr. Scott, Mr. Ayres and Dr. Thornton, three of whom we've already heard about.

MR. CIRESI: Your Honor, we would offer Exhibit 11259.

MR. BERNICK: No objection, Your Honor.

THE COURT: As I read it, it's the 16th of February, not the 18th; is that correct?

MR. CIRESI: That's the --

The meeting, Your Honor, the document on the last page under Mr. Blackman's signature says 18 February 1983.

THE COURT: Okay. All right, the court will receive 11259.

BY MR. CIRESI:

Q. Doctor, first of all, what was the meeting about? Is that referenced in this document in the first paragraph?

A. Well they were discussing eleven research proposals contained in the ISC 3rd Report, so this is a group of people developing a response, as I understand it, to these research proposals that had been put before them.

Q. And does Dr. Blackman in the second paragraph make reference to the type of response that should be forthcoming from the industry?

A. Well he points out that "Although some of the research areas that are proposed are commercially

sensitive, the TAC," which is the Tobacco Advisory Committee, "response must be seen -- must be seen by the ISC to be constructive." So "A series of, quote, no comment, unquote, will surely provoke aggression and hinder future voluntary agreements."

Q. Now in the third paragraph does Dr. Blackman reference the fact that there are dangers for the industry to be seen to work in collaboration with the ISC, which is the Independent Scientific Committee?

A. He does say that. He says, "There are, however, dangers for the industry to be seen to work in collaboration with the ISC; and also possible legal implications for the industry seemingly to accept the concept underlying some of the research proposals."

Q. And with regard to the role of nicotine in these research proposals, can you turn to page three, paragraph five. And is the issue of the role of nicotine and any collaborative effort with the Independent Scientific Committee addressed in that issue?

A. Yes, it's addressed quite directly.

Q. What does Dr. Blackman say?

A. Well this subtitle on this is "The role of nicotine, at the relevant lower range of nicotine dosage, in perpetuating the smoking habit." So this

is, again, talking about coming near this bottom threshold of dosage and being concerned about whether or not, if it goes too low, then you lose the -- its habit-forming effects, would no longer perpetuate the habit. So he points out that much information already exists in the literature. He cites some people, and this is a particularly sensitive area for the industry. It says, "If any future study showed that nicotine either was, or was not, associated with perpetuating the smoking habit, industry could well be called upon to reduce or eliminate nicotine from the product." And it goes on to say, this is "A heads we lose, tails we cannot win situation."

And restating that, what he's -- what he's saying is that if nicotine was associated with perpetuating the smoking habit, they might be called on to reduce it, and if it wasn't, they might be called on to reduce it anyway. So it seems like a no-win situation.

So it goes on to say, "We must not become involved in any collaborative study with the ISC."

Q. Now doctor, were there other documents of the defendants that dealt with this threshold issue of nicotine and how low you could go?

A. Yes, there were many, many such documents.

Q. And is a drug-dose window essential to a drug-delivery device?

A. Well it's -- it's -- it's key because it defines where the device should exist. If you -- if you don't have the drug, then you don't need to talk about a dose window, but then if you don't have a drug, you don't have a delivery system, so it kind of compounds itself. So it's absolutely a requirement to -- to know of it and to identify it.

Q. Now with regard to nicotine and its taste, were there a number of documents of the defendants that addressed the issue of the taste of nicotine in the collection of documents that you reviewed?

A. Yes, there were many, many such documents.

Q. Can you direct your attention to Exhibit 12673. This is an RJR document, subject, "Nicotine Research," date November 9th, 1976, it's do Dr. D. H. Piehl from W. M. Henley, H-e-n-l-e-y, and on the back page you'll see that it goes to a number of individuals, including some that we've heard about already such as Dr. Rodgman.

Is this one of the documents that you reviewed with respect to forming the basis of your opinion in this case?

A. Yes, it is.

Q. And is it representative of the defendants'

documents that you reviewed regarding the subject matters upon which you're testifying?
A. Yes.
MR. CIRESI: Your Honor, we would offer Exhibit 12673.
MR. BERNICK: No objection, Your Honor.
THE COURT: Court will receive 12673.
BY MR. CIRESI:
Q. If we could have the first page first. It shows the subject matter in the upper left-hand corner, "Nicotine Research," the date of November 9th, 1976, the author, Mr. Henley, and the addressee, Dr. Piehl, and on the last page is a list of the recipients of this memorandum starting with Dr. Alan Rodgman.
Now if we go back to the first page, doctor, does this paper address the summary of the major points that were developed during an October 25th, 1976 discussion on nicotine?
A. Yes.
Q. And are the topics that were discussed listed next to the principal participants with regard to each one of those subjects?
A. Yes. There's six topics listed.
Q. And they include the physiological action of

nicotine?
A. Yes.
Q. Smoking and health aspects?
A. Right.
Q. Taste of nicotine?
A. Yes.
Q. Factors influencing presence in leaf and smoke?
A. Yes.
Q. Nicotine and tobacco substitutes?
A. Right.
Q. And finally nicotine analogs and mimics; is that correct?
A. Yes.
Q. What's an analog?
A. Something that behaves like nicotine, in this particular case nicotine, a substitute for it that has the same kind of behavior.
Q. Under Roman numeral I, "Physiological Action of Nicotine," does it set forth the site of the nicotine action in the brain?
A. Yes, it describes nicotine interaction with the cholinoceptive receptors at neural junction and thus initiating normal neural impulses.
Q. And if we go over to page two under paragraph two, does it refer to the absorption, metabolism and

excretion of nicotine?
Halfway down, doctor.
A. Oh, number two. Sorry.
Q. Yes.
A. Absorption, metabolism, excretion, yes.
Q. And does it address how effective cigarette

smoke is in administering nicotine?
A. Oh, it says it's the most -- it's probably the most effective method of administering nicotine to the body, is by inhalation of cigarette smoke.
Q. And is this what you found the rest of the defendants also held an opinion on based on your review of their documents?
A. Yes.
Q. And in that paragraph does it reference the speed within which the nicotine can get to the brain?
A. Yes. It says, "Thus a high concentration of nicotine is suddenly produced in the pulmonary veins, which is then distributed to the brain and many parts of the body within a few seconds."
Q. And does it contrast the amount of nicotine needed to get the same levels if one were to do it by intravenous as opposed to inhalation?
A. It points out that "Efforts to reproduce this concentration of blood nicotine," that is, the

concentration achieved by inhalation, the "Efforts to reproduce this concentration of blood nicotine by intravenous injection usually require about twice the amount of nicotine injected versus inhaled to produce a given physiologic response."
Q. And can you direct your attention over to page three under "Taste of Nicotine." Is there a reference there to the presentation made to the various scientists at RJR with regard to the taste of nicotine?
A. Yes. This was a report where, apparently, different strength solutions of nicotine added to water were -- were tasted, and at concentrations of what's called ten to the minus five molar, means -- it's a decimal point with four zeroes and a five, it's a small, small number -- ten to the minus six would be one millionth, so this is ten times one millionth. And a molar you can see in that case is 1.62 micrograms per ml, that's how much nicotine was in the -- in the liquid to --
What that means is it's 1.2 -- 1.62 millionths of a gram in one gram of water, and there was no taste perception. At ten times that level, which would be about 16 millionths of a gram in one gram of water -- and one gram of water is a very small amount

of water -- there's some taste, and they described it as being foul and like rotten rubber. And then they go on to describe what happens as you increase the concentration.
So it was a very low taste threshold, the point that's coming across here.
Q. And if you direct your attention to the next page, is there reported in this research memorandum what was told the assembled scientists from RJR with regard to how nicotine is handled in a cigarette smoke with regard to its taste?

A. Well they finally get to the point where he says, "Nicotine is definitely an irritant," we've seen that before already today, "is definitely an irritant in smoke and its taste must be blended out or modified by other constituents in the TPM," which is total particulate matter, which is basically like the tar we've been talking about, "to make the smoke acceptable."

So you're -- the product that you want to deliver is irritating and tastes bad, so what one has to do is mask that taste somehow in order to make it palatable to the consumer.

Q. And did you find statements like that in other of the defendants' documents?

A. Yes, I did.

Q. Can you direct your attention to Exhibit 10529, which also deals with the taste subject. It's a Philip Morris document. This is a document dated March 24th, 1980. It's to Dr. Seligman, vice-president of research and development -- we've heard from him before -- from W. L. Dunn, subject, "High Nicotine, Low TPM Cigarettes."

Is this one of the documents you reviewed, doctor?

A. Yes.

Q. And does it form part of the basis of your opinion with regard to the opinions you've rendered in this case and will render?

A. Yes.

MR. CIRESI: We would offer, Your Honor, Exhibit 10529.

MR. BERNICK: No objection.

THE COURT: Court will receive 10529.

BY MR. CIRESI:

Q. First of all in the first paragraph, does Mr. Dunn reference the harshness of nicotine as it relates to the nicotine/tar ratio?

A. Yes. He points out that there's a lack of -- of acceptance of high N/T, that means nicotine-to-tar

ratio, so high nicotine-to-tar ratio could be achieved by either elevating the nicotine or lowering the tar relative to the nicotine. In either case the ratio is going up, so there's going to be more nicotine relative to tar. It says a lack of acceptance of high nicotine-to-tar ratios may be due to harshness or taste unpleasantness, but that it could be masked, implying that if such masking could be achieved, then perhaps higher nicotine-to-tar ratios would be marketable. And you see this is consistent with the tar levels dropping and the nicotine levels dropping, having to keep the nicotine level from going through this lower threshold. If you keep the nicotine up as tar continues to drop, then the nicotine-to-tar ratio will start increasing. So that's what they're talking about here.

Q. And in the last paragraph of this memorandum, does Mr. Dunn address the issue of the taste problem of nicotine?
A. Yes. He says, "As a point of reference I think in terms of a 5 milligram cigarette," this meaning the level of tar, "delivering .75 milligrams to 1 milligram of nicotine, the task being to overcome the taste problem typically reported with such a preponderance of nicotine."

So this would be a -- a cigarette that would be delivering a small amount of tar and yet an amount of nicotine which, relative to that tar, is -- is high, and so this would be a high nicotine-to-tar ratio cigarette, and they would anticipate problems with taste that would have to be overcome.
Q. Doctor, could you now direct your attention to Exhibit 13555, which is a B&W and B.A.T document dated 12-24-52. This is Exhibit 13555.
The document is stamped "CONFIDENTIAL" with a date is 24 December, 1952, it's entitled "REPORT OF PROGRESS - TECHNICAL RESEARCH DEPARTMENT."
Is this one of the documents that you reviewed in this case?
A. Yes.
Q. Does it form part of the basis of your opinion?
A. It does.
Q. Is it consistent and representative with the documents of the other defendants that you reviewed in this case concerning the subject matter of taste of nicotine?
A. Yes.
MR. CIRESI: Your Honor, we would offer Exhibit 13555.
MR. BERNICK: No objection.

THE COURT: Court will receive 13555.
BY MR. CIRESI:
Q. It's hard to make out the title, but it says "REPORT OF PROGRESS - TECHNICAL RESEARCH DEPARTMENT, 24 December 1952." And if you could, doctor, would you direct your attention to page eight of that document. This is a continuation --
Maybe we could put up the previous page. I'm sorry.
The paragraph that we're in is Roman numeral IX, "TOBACCO SMOKE, The investigation of the chemical composition and the physiological effects of tobacco smoke has been continued along the following lines," number one, "The Chemical Composition." And then we go over to the next page, and at the top of that page is the issue of taste of nicotine addressed?
A. Yes, it is.
Q. And where is that, sir?
A. It says, "A literature search has revealed that among approximately forty-nine individually known compounds (not including the casing materials) there

exists approximately sixteen different functional groups which contribute directly or indirectly to the final 'conglomerate' taste of tobacco smoke. From these sixteen classes of compounds, which were tested

by a smoker-test panel, it appears that aldehydes," which is a class of chemicals, "alkaloids, heterocycles and amines contribute the most to the undesirable taste and irritation of tobacco smoke." Nicotine is an alkaloid.

Q. And doctor, finally on this subject, can you direct your attention to Exhibit 12749, which is an R. J. Reynolds document dated 5-5-83. 12749. This is a memorandum dated May 5th, 1983, the subject is an "Interview with John L. McKenzie," it's to the Sensory Modeling Committee, it's from Mary E. Stowe and J. P. Dickerson.

Is this one of the documents that you reviewed?

A. Yes, it is.

Q. And does it form part of the basis of your opinion?

A. Yes.

Q. And is it representative of the other documents that you reviewed with regard to the subject matters contain therein?

A. Yes.

MR. CIRESI: Your Honor, we would offer Exhibit 12749.

MR. BERNICK: No objection.

THE COURT: Court will receive 12749.

BY MR. CIRESI:

Q. Do you see at the top it's -- the subject was "Interview with John L. McKenzie," to the Sensory Modeling Committee, the date is May 5th, 1983, it's from Mary Stowe and J. P. Dickerson, and if we go over to page two, you will see that carbon copies were sent to a number of other individuals at Reynolds. And if we could go to the top of this document on page two, is there a reference to nicotine's taste?

A. Yes. This is a list of what are considered general perceptions on the effects of specific cigarette variables on smoking quality, and points out that nicotine is harsh and it's bitter.

Q. And doctor, were there other documents that you reviewed from the defendants' files, the collection that you reviewed, which related to the taste of nicotine?

A. Yes.

Q. And were those documents consistent with the documents you reviewed here today?

A. They were.

Q. Now doctor, based upon your education, experience, expertise, and review of the defendants' documents, do you have a opinion to a reasonable

degree of scientific certainty whether a cigarette is a drug-delivery device?
A. Yes, I do.
Q. And what is your opinion?
A. It is a drug-delivery device.
Q. And what is the basis of your opinion, doctor?
A. The basis is that the defendants knew that nicotine is a drug, they knew that there was a lower threshold for its pharmacologic activity above which the device had to operate in order to be successful, they knew that if they removed the nicotine, thereby violating the lower threshold, they'd have no business. A cigarette contains all the elements of a drug-delivery device.
Q. Doctor, we have both an overhead and a blowup for illustrative purposes only, and maybe you could come down and just describe the elements of the drug-delivery system and which portion of the cigarette relate to which element.
A. You'll recall earlier today we talked about the elements that are found in drug-delivery devices, and now to apply this to a cigarette to see if it has those elements, where the elements are, and how they come together to give us this drug-delivery device.
So number one is their platform, and the answer

to that question is yes. The platform is the cigarette itself. It holds and contains all of the elements.
THE WITNESS: Is -- do you have it on the TV?
THE COURT: Yes, I have it right here.
A. It has a reservoir; that is, there's a place where the drug is stored, and it's stored in the tobacco material that's contained in the tobacco rod.
Is there a portal? Is there a place for the drug to be released into the recipient, into the human body? And yes, there is, and that's at the filter end of this cigarette, which is a filter cigarette where you grip it in your mouth and you suck and puff in the drug.
Is there an energy source which allows the drug to move from the reservoir through the portal and into the recipient? And yes, once the cigarette is lit, the combustion process and the heat associated with it causes a liberation of the nicotine from the tobacco product and then, to direct it into your body, you suck on the tobacco rod, and then that draws the smoke aerosol through the rod and into your mouth. So basically the human provides the energy source to bring the tobacco smoke into the body.

And is there a rate controller? The primary rate controller is the smoker themselves because,

depending on how hard they draw, how big a puff they take, how often they puff, how far they choose to smoke the cigarette, will determine the drug intake. And since that is determined by the smoker responding to the device, a cigarette is a total feedback control system in terms of a drug-delivery device.

Q. Thank you, doctor.

MR. CIRESI: Record should reflect that Dr. Robertson was reviewed -- or was referring, excuse me, to Exhibit 30232. And we would offer that for illustrative purposes only, Your Honor.

MR. BERNICK: I have no objection to that, Your Honor.

THE COURT: I'm sorry, was that 322?

MR. CIRESI: 30232, Your Honor.

BY MR. CIRESI:

Q. Doctor, we're going to move to a new subject matter now, and that is the various component parts of a cigarette. And I guess I shouldn't have let you sit down because I was going to use another illustrative --

MR. CIRESI: Your Honor, we are moving to a new subject and this will take some time.

THE COURT: Maybe we should recess at this time.

MR. CIRESI: All right.

THE COURT: And adjourn until 9:30 tomorrow morning. Again, keep in mind my admonition: Don't go home and talk to your spouses about the case. Okay? We'll recess.

THE CLERK: Court stands in recess.

(Recess taken.)